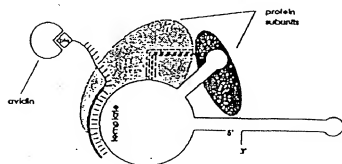
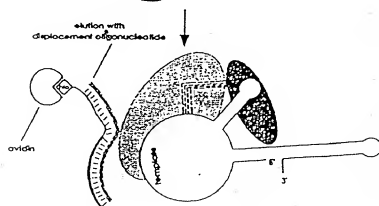


FIGURE 1

PANEL A



PANEL B



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FIGURE 2

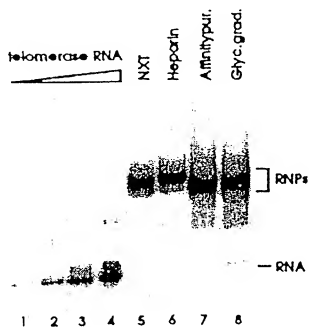


FIGURE 3

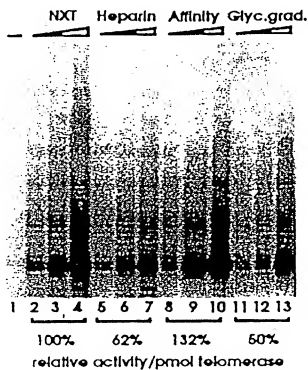


FIGURE 4

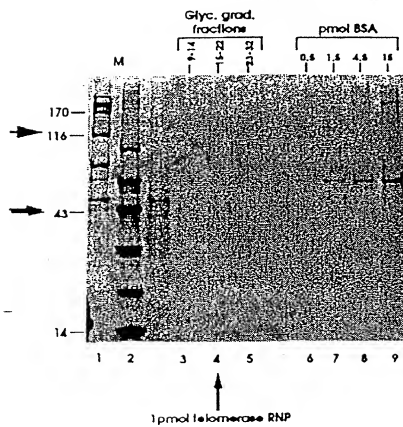


FIGURE 5

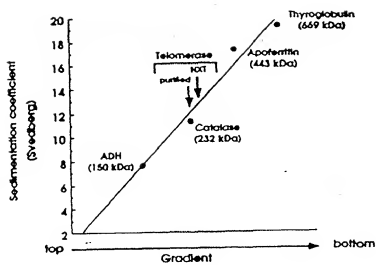
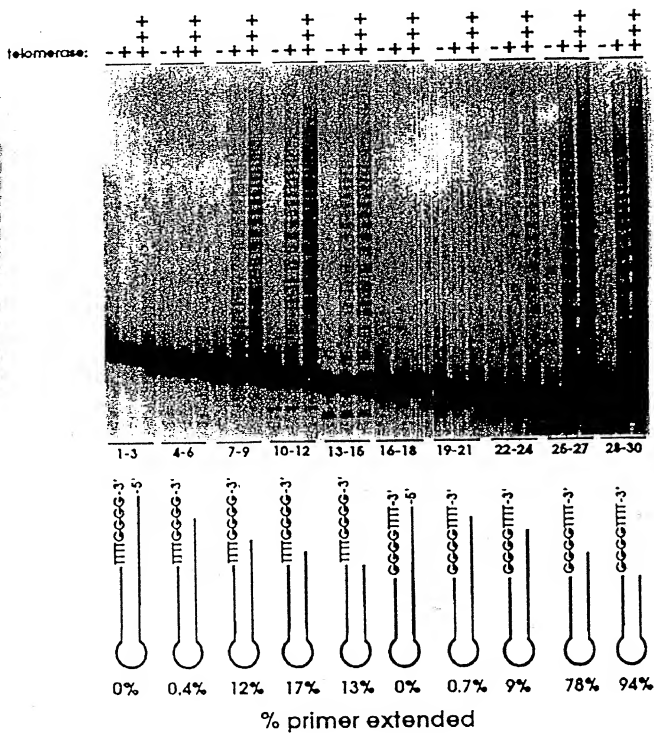


FIGURE 6



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FIGURE 7

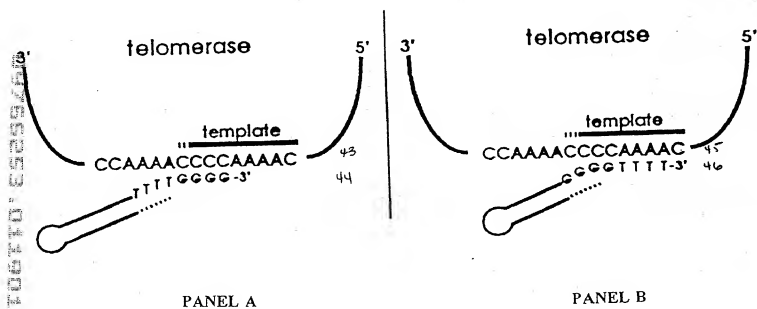
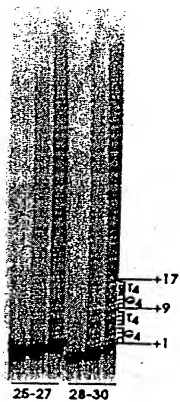


FIGURE 8



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FIGURE 9

1 AAAACCCCAA AACCCCAAAA CCCCTTTTAG AGCCCTGCG AGTTGAAATAT  
51 AACCTCAGTA TTAATAAGCT CAGATTTTAA ATATTAATTA CAAAACCTAA  
101 ATGGAGGTTG ATGTTGATAA TCAAGCTGAT AATCATGGCA TTCACCTCAGC  
151 TCTTAAGACT TGTGAAGAAA TTAAGAAGC TAAACCGTTG TACTCTTGGA  
201 TCCGAAGAAGT TATTAGATGA AGAAATCAAT CTCAAAGTCA TTATAAAGAT  
251 TTAGAAGATA TAAAAATATT TGCGCAGACA AATATTGTG CTACTCCAGC  
301 AGACTATAAT GAAGAAGATT TTAAGTTAT TGCAAGAAAA GAAGTATTTT  
351 CAACCTGGACT AATGATCGAA CTTATTGACA AATGCTTAGT TGAACCTCTT  
401 TCATCAAGCG ATGTTTCAGA TAGACAAAAA CTTCAATGAT TTGGATTTC  
451 ACTTAAGGGA AATCAATTAG CAAAGACCCA TTTATTAACA GCTCTTTCAA  
501 CTCAAAAGCA GTATTTCTTT CAAGACGAAT GGAACCAAGT TAGAGCAATG  
551 ATTGGAATG AGCTCTTCG ACATCTCTAC ACTAAATATT TAATATTCCA  
601 GCGAATCTCT GAAGGAAGCT TTGTTCAATT TTGCGGGAAT AACGTTTTTG  
651 ATCATTGAA AGTCAACGAT AAGTTTGACA AAAAGCAAAA AGGTGGAGCA  
701 GCAGACATGA ATGAACCTCG ATGTTGATCA ACCTGCAAT ACAATGTCAA  
751 GAATGAGAAA GATCACTTTC TCAACAACAT CAACGTGCCG AATTGGAATA  
801 ATATGAATC AAGAACCAGA ATATTTTAT GCACATATT TAATAGAAAT  
851 AACCAATTCT TCAAAAAGCA TGAGTTTGTG AGTAACAAAA ACAATATTTT  
901 AGCGATTGGAC AGAGCTCAGA CGATATTCAC GAATATATTC AGATTTAATA  
951 GAATTAGAAA GAAGCTAAAA GATAAGTTA TCGAAAAAAT TGCTACATG  
1001 CTTGAGAAAG TCAAAGATTT TAACCTCAAC TACTATTTAA CAAAACTTG  
1051 TCCTCTTCCA GAAAAATGGC GGAACCGAA ACAAAAAATC GAAAACTTGA  
1101 TAAATAAAAC TAGAGAAGAA AAGTCGAAGT ACTATGAAGA GCTGTTTAGC  
1151 TACACAACGT ATAATAAATG CGTCACACAA TTTATTAATG AATTTTCTA  
1201 CAATATACTC CCCAAAGACT TTTTGACTGG AAGAAACCGT AAGAATTTTC  
1251 AAAAGAAAGT TAAGAAATAT GTGGAACATA ACAAGCATGA ACTCATTAC  
1301 AAAAACCATT TGCTTGAGAA GATCAATACA AGAGAAATAT CATGGATGCA  
1351 GGTGAGACC TCTGCAAAGC ATTTTATTA TTTTGATCAC GAAACACATC  
1401 ACGCTTTATG GAAATTGCTC CGATGGATAT TCGAGGATCT CGTCGTCTCG  
1451 CTGATTAGAT GATTTTCTA TGTCACCGAG CAACAGAAAA GTTACTCCAA  
1501 AACCTATTAC TACAGAAAGA ATATTGGGA CGTCATTATG AAAATGTCAA  
1551 TCGGAGACTT AAGAAGGAA ACGCTTGCTG AGGTCCAAGA AAAAGAGGTT  
1601 GAAGAATGGA AAAAGTCGCT TGGATTGCA CTGGAAGAAC TCAGACTAAT  
1651 ACCGAAGAAA ACTACTTTCC GTCCAATTAT GACTTTCAAT AAGAAGATTG  
1701 TAAATTGAGA CCGGAAGACT ACAAATTAA CTACAAATAC GAAGTATTG  
1751 AACTCTCACT TAATGCTTAA GACATTGAAG AATAGAATGT TAAAGATCC  
1801 TTTTGGATTG CGTGTTTTTA ACTATGATGA TGTAATGAAA AAGTATGAG  
1851 AGTTTGTGTT CAAATGGGAA CAAGTTGGAC AACCAAACT CTCTTTGCA  
1901 ACTATGGATA TCGAAAAGTG ATATGATAGT GTAAACAGAG AAAAAGATC  
1951 AACACTCTTA AAAAACTACTA AATTACTTTC TTCAAGATTTC TGATTATGA  
2001 CTGCACAAAT TCTAAAGAGA AAGAATAACA TAGTTATCGA TTCGAAAAAC  
2051 TTGAGAAAAA AAGAATGAA AGATTATTTT AGACAGAAAT TCCAGAAGAT  
2101 TGACATTGAA GGAGGACAAT ATCCAACCTT ATTCAGTGT CTTGAAATG  
2151 AACAAAAATGA CTAAATGCA AAGAAAACAT TAATTGTTGA AGCAAGGCAA  
2201 AGAAATTTAT TTAAGAAAGA TAACCTTACT CAACCAAGTCA TTAATATTTG  
2251 CCAATATAAT TACATTAECT TTAATGGGAA GTTTTATAAA CAAACAAAAAG  
2301 GAATTCCTCA AGGTCTTTGA GTTTCATCAA TTTTGTATC ATTTTATTAT

FIGURE 9 (cont.)

2351 GCAACATTAG AGGAAAGCTC CTTAGGATTC CTTAGAGATG AATCAATGAA  
2401 CCCTGAAAAT CCAAATGTTA ATCTTCTAAT GAGACTTACA GATGACTATC  
2451 TTTTGATTAC AACTCAAGAG AATAATGCAG TATTGTTTAT TGAGAAACTT  
2501 ATAAACGTAA GTCGTGAAAA TGGATTTAAA TTCAATATGA AGAAACTACA  
2551 GACTAGTTTT CCATTAAGTC CAAGCAAATT TGCAAAATAC GGAATGGATA  
2601 GTGTTGAGGA GCAAAATATT GTTCAAGATT ACTGCGATTG GATTGGCATC  
2651 TCAATTGATA TGAAAACCTCT TGCTTTAATG CCAAATATTA ACTTGAGAAT  
2701 AGAAGGAATT CTGTGTACAC TCAATCTAAA CATGCAAAAC AAGAAAAGCAT  
2751 CAATGTGGCT CAAGAAGAAA CTAAAGTCGT TTTAATGAA TAACATTACC  
2801 CATTATTTTA GAAAGACGAT TACAACCGAA GACTTTGCGA ATAAAACTCT  
2851 CAACAAGTTA TTTATATCAG GCGGTTACAA ATACATGCAA TGAGCCAAAG  
2901 AATACAAGGA CCACITTAAG AAGAACITAG CTATGAGCAG TATGATCGAC  
2951 TTAGAGGTAT CTAATATTAT ATACTCTGTA ACCAGAGCAT TCTTTAATA  
3001 CCTTGTGTGC AATATTAAGG ATACAATTTT TGGAGAGGAG CATTATCCAG  
3051 ACTTTTTCTT TAGCACACTG AAGCACTTTA TTGAAATATT CAGCACAAAA  
3101 AAGTACATTT TCAACAGAGT TTGCATGATC CTCAGGCAA AAGAAGCAAA  
3151 GCTAAAAAGT GACCAATGTC AATCTCTAAT TCAATATGAT GCATAGTCGA  
3201 CTATTTCTAAC TTATTTTGGG AAGTTAATTT TCAATTTTGG TCTTATATAC  
3251 TGGGGTTTGG GGGTTTGGG GTTTTGGG



FIGURE 11

1 CCCCCAAACC CCAAAACCCC AAAACCCCTA TAAAAAAGA AAAAATTGAG  
 51 GTAGTTTGA AATAAAATAT TATTCCCGCA CAAATGGAGA TGGATATTGA  
 101 TTTGGATGAT ATAGAAAATT TACTTCTTAA TACATTCAAC AAGTATAGCA  
 151 GCTCTTGTAG TGACAAGAAA GGATGCAAAA CATTGAAATC TGGCTCGAAA  
 201 TCGCCTTCTG TACTATTCC AAAGTTGCAA AAACAATTAG AGTCTTACTT  
 251 CTCGGATGCA AATCTTTATA ACGATTCTTT CTTGAGAAAA TTAGTTTAA  
 301 AAAGCGGAGA GCAAAGAGTA GAAATTGAAA CATTACTAAT GTTTAAATAA  
 351 AATCAGGTAA TGAGGATTAT TCTATTTTTT AGATCACTTC TTAAGGAGCA  
 401 TTATGGAGAA AATTACTTAA TACTAAAAGG TAAACAGTTT GGATTATTTC  
 451 CCTAGCCAAC AATGATGAGT ATATTTAAAT CATATGAGAA TGAGTCAAAG  
 501 GATCTCGATA CATCAGACTT ACCAAAGACA AACTCGCTAT AAAACGCAAG  
 551 AAAAAGTTTG ATAATCGAAC AGCAGAAGAA CTTATTGCAT TTACTATTCTG  
 601 TATGGGTTTT ATTACAATTG TTTTAGGTAT CGACGGTGAA CTCCCGAGTC  
 651 TTGAGACAAT TGAAAAAGCT GTTTACAACG GAAGGAATCG CAGTTCTGAA  
 701 AGTTCTGATG TGTATGCCAT TATTTTGTGA ATTAATCTCA AATATCTTAT  
 751 CTCAATTTAA TGGATAGCTA TAGAAACAAA CCAATAAAC CATGCAAGTT  
 801 TAATGGAATA TACGTTAAAT CCTTTGGGAC AAATGCACAC TGAATTTATA  
 851 TTGGATTCTT AAAGCATAGA TACACAGAAT GCTTAGAGA CTGATTTAGC  
 901 TTACAACAGA TTACCTGTTT TGATTACTCT TGCTCATCTC TTATATCTTT  
 951 AAAAGAAGCA GCGGAAATGA AAAGAAGACT AAAGAAAGAG ATTTCAAAAT  
 1001 TTGTTGATTCT TTCTGTAACC GGAATTAACA ACAAGAATAT TAGCAACGAA  
 1051 AAAGAAGAAG AGCTATCACA ATCCTGATTCT TAAAGATTCT CAAAAATTCC  
 1101 AGGTAAGAGA GATACATTCA TAAAAATCA TATATTATAG TTTTTCATT  
 1151 CACAGCTGTT ATTTTCTTTT ATCTTAACAA TATTTTITGA TTAGCTGGAA  
 1201 GTAAAAAGTA TCAAATAAGA GAAGCGCTAG ACTGAGGTAA CTTAGCTTAT  
 1251 TCACATTCAAT AGATCGACCT TCATATATCC AATACGATGA TAAGGAAACA  
 1301 GCAGTCATCC GTTTTAAAAA TAGTGCTATG AGGACTAAAT TTTTAGAGTC  
 1351 AAGAAATGGA GCCGAAATCT TAATCAAAAA GAATTGCGTC GATATTGCAA  
 1401 AAGAATCGAA CTCTAAATCT TTCGTTAATA AGTATTACCA ATCTTGATTG  
 1451 ATTGAAGAGA TTGACGAGGC AACTGCACAG AAGATCATT AAGAAATAAA  
 1501 GTAACTTTTT TTAATTAGAG AATAAACTAA ATTACTAATA TAGAGATCAG  
 1551 CGATCTTCAA TTGACGAAAT AAAAGCTGAA CTAAGTTTGA ACAATAAAAA  
 1601 ATACAAACCT TGGTCAAAAT ATTGAGGAAG GAAAAGAAGA CCAGTTAGCA  
 1651 AAAGAAAAAA TAAGGCAATA AATAAAATGA GTACAGAAGT GAAGAAATAA  
 1701 AAGATTTATT TTTTCAATA ATTTATTGAA AAGAGGGGTT TTGGGGTTTT  
 1751 GGGGTTTTGG GG

FIGURE 12

1 CCCCCAACCCCAAAACCCCAAAACCCCTATAAAAAAGAAAAAATGAGGTAGTTTAGA 60  
 GGGGTTTTGGGTTTTGGGTTTTGGGGATATTTTTTCTTTTAACTCCATCAATCT  
 a P O N P K T P K P L \* K K K K L R \* F R -  
 b P K T P K P O N P Y K K R K N C G S L E -  
 c P K P O N P K T P I K K E K I E V V \* K -  
 61 AATAAAATATTATCCCGCACAAATGGAGATGGATATTGATTGGATGATATAGAAAAT 120  
 TTATTTTATAATAAGGCGTGTTTACCTCTACCTATAACTAACTACTATATCTTTAA  
 a N K I L F P P H K W R W I L I W M I \* K I -  
 b I K Y Y S R T N G D G Y C F G C Y R K K F -  
 c \* N I I P A Q M E M D I D L D D I E N L -  
 121 TACTTCTAATACATTCAACAAGTATAGCAGCTCTTGTAGTGACAAGAAAGGATCAAAA 180  
 ATGAAGGATTATGTAAGTTGTTTCATATCGTCGAGAACATCACTGTTCTTTCACGTTTT  
 a Y P L I H S T S I A A L V V T R K D A K -  
 b T S \* Y I Q Q V \* Q L L \* \* Q E R M Q N -  
 c L F N T F N K Y S S S C S D K K G C K T -  
 181 CATTGAAATCTGGCTCGAAATCGCCTTCATTGACTATTCCAAAGTTGCAAAAACAATTAG 240  
 GTAACTTTAGACCGAGCTTTAGCGGAAGTAACGTATAAGGTTTCAACGTTTTTGTGAATC  
 a H C N L A R N R L H C L F Q S C K N N \* -  
 b I E I W L E I A F I D Y S K V A C T I R -  
 c L K S G S K S P S L T I P K L Q K Q L E -  
 241 AGTTCTACTTCTGGATGCAAACTTTATAACGATCTTTCTTGAGAAAAATAGTTTAA 300  
 TCAAGATGAAGAGCCTACGTTTGAATAATGCTAAGAAAGAACTCTTTAATCAAAAT  
 a S S T S R M Q I F I T I L S C E N \* F \* -  
 b V L L L G C K S L \* R F F L E K I S F K -  
 c F Y F S D A N L Y N D S F L R K L V L K -  
 301 AAAGCGGAGAGCAAGACTAGAAATGAACACTTAACTATTTAAATAAAAATCAGGTAA 360  
 TTTCGCCCTCGTTTCTCATCTTTAACTTTGTAATGATTACAAAATTTATTAGTCGATT  
 a K A E S K E \* K L K H Y \* C L N K I R \* -  
 b K R R A K S R N C N I T N V \* I K S G N -  
 c S G E Q R V E I E T L L M F K \* N Q V M -  
 361 TGAGGATTATTCTATTTTATGATCACTTCTTAAAGGAGCATTTGAGAGAAAATACTTAA 420  
 ACTCTAATAAGATAAAAAATCTAGTGAAGAATTCCTCGTAATACCTCTTTTAAAGAAAT  
 a C G L F Y F L D H F L R S I M E K I T \* -  
 b E D Y S I F \* I T S \* G A L W R K L L N -  
 c R I I L F F R S L L K E H Y C E N Y L I -  
 421 TACTAAAAAGGTAAACAGTTTGGATTATTTCCCTAGCCAACAATGATGAGTATATTAAT 480  
 ATGATTTTCCATTTGTCAAACCTAATAAAGGATCGGTTCTTACTACTCATATAATTTAA  
 a Y \* K V N S L D Y F P S Q Q C C V Y \* I -  
 b T K R \* T V W I I S L A N N D E Y I K F -  
 c L K G K Q F G L F P \* P T H M S I L N S -

FIGURE 12 (cont.)

CATATGAGAATGAGTCAAAGGATCTCGATACATCAGACTTACCAAAGACAAACTCGCTAT  
 481 -----+ 540  
 GTATACTCTTACTCAGTTTCTTAGAGCTATGTAGTCTGAATGGTTTCTGTTTGAGCGATA  
 a H M R M S Q R I S I H Q T Y Q R Q T R Y -  
 b I C E C V K G S R Y I R L T K D K L A I -  
 c Y E N E S K D L D T S D L P K T N S L -  
 AAAACGCAAGAAAAGTTTGTAATCGAACAGCAGAGAAGAACTTATGCTTACCTCG  
 541 -----+ 600  
 TTTTGGCTTCTTTTCAAACATATAGCTTGTGCTTCTTGAATAACGTAATGATAAGC  
 a K T Q E K V C \* S N S R R T Y C I Y Y S -  
 b K R K K K F D N R T A E E L I A F T I R -  
 c N A R K S L I I E Q Q K N L L H L L F V -  
 TATGGGTTTTATTACAAATGTTTTAGGTATCGACGGTGAACCTCCCGAGTCTTGAGACAAT  
 601 -----+ 660  
 ATACCCAAAATAATGTTAACAAAATCCATAGCTGCCACTTGAGGGCTCAGAATCTGTTA  
 a Y G F Y Y N C F R Y R R R C T P E S C D N -  
 b M G F I T I V L G I D G E L P S L E T I -  
 c W V L L Q L F \* V S T V N S R V L R Q L -  
 TGAAAAGCTGTTTACAACTGAAGGAATCGCAGTCTGAAAGTCTGATGTGTATGCCAT  
 661 -----+ 720  
 ACTTTTTCGACAAATGTTGACTTCTCTTAGCTCAAGACTTTCAGAGCTACACATACGGTA  
 a C K S C L Q L K E S O F C K F \* C V C H -  
 b E K A V Y N C R N R S S E S S D V Y A I -  
 c K L L F T T E G I A V L K V L C M P L -  
 TATTTTGTGAATTAATCTCAAATATCTTATCTCAATTTAATGGATAGCTATAGAAACAAA  
 721 -----+ 780  
 ATAAACACTTAATAGAGTTTATAGAAATAGAGTTAAATTACCTATCGATCTCTTGTTT  
 a Y F V N \* S O I S Y L N L M D S Y R N K -  
 b I L C I N L K Y L I S I \* W I A I E T N -  
 c F C E L I S N I L S O F N G \* L \* K Q T -  
 CCAATTAACCATGCAAGTTTAATGGAATATACGTTAAATCTTTGGGACAAATGACAC  
 781 -----+ 840  
 GGTTTATTTGGTACGTTCAAATTACCTTATATGCAATTTAGGAAACCTGTTTACGCTGT  
 a P N K P C K F N G I Y V K S F G T N A H -  
 b Q I N H A S L M E Y T L N P L G O M H T -  
 c K \* T M Q V \* W N I R \* I L W D K C T L -  
 TGAATTTATATTGATCTTTAAAGCATAGATACACAGAATGCTTTAGAGACTGATTAGC  
 841 -----+ 900  
 ACTTAAATATAACCTAAGAATTCGTATCTATGTGTCTTACGAATCTCTGACTAAATCG  
 a C I Y I G F L K H R Y T E C F R D C F S -  
 b E F I L D S \* S I O T Q N A L E T D L A -  
 c N L Y W I L K A \* I H R H L \* R L I \* L -  
 TTACAACAGATTACCTGTTTGTATTACTCTTGCTCATCTTTATATCTTTAAAAGAGCA  
 901 -----+ 960  
 AATGTTGTCTAATGACAAAACATAAGAGAGAGTATAGAAAATTTCTTCGT  
 a L Q O I T C F D Y S C S S L I S L K E A -  
 b Y N R L P V L I T L A H L L L Y L \* K K Q -  
 c T D Y L F C L L L L I S Y I F K R S R -  
 GCGGAATGAAGAAAGACTAAAGAAAGAGATTCAAATTTGTTGATCTTCTGTAACC  
 961 -----+ 1020  
 CCGCTTACTTTTCTCTGATTCTTCTCTTAAAGTTTAAACAACTAAGAGAGACTTGG  
 a G E N K R R L K K E I S K F V D S S V T -  
 b A K C K E D \* R K R F Q N L L I L L \* P -  
 c R N E K K T K E R D F K I C C F F C N R -  
 GGAATTAACAAGAATATTAGCAACGAAAAGAGAGAGCTATCAACAATCTCGATTTC  
 1021 -----+ 1080  
 CTTAATTTGTTGCTTATAATCGTTGCTTTTCTTCTTCTCGATAGTGTAGGACTAAG  
 a G I N N K N : S N E K E E E L S Q S C F -  
 b E L T T R I L A T K K K K S Y H N P D S -  
 c N \* Q Q E Y \* Q R K R R R A I T I L I L -

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FIGURE 12 (cont.)

1081 TTAAGGATTTCAAAATTCAGGTAAGAGAGATACATTCATTAAAATTCATATATTATAG 1140  
AATTTCTAAAGTTTTAAAGTCCATTCTCTCTATGTAAAGTAATTTAAGTATATAATATC

a b c  
L K I S K I P G K R D T F I K I H I L \* -  
\* R F O K F Q V R E I H S L K F I Y Y S -  
K D F K N S R \* E R Y I H \* N S Y I I V -

1141 TTTTTCATTTCACAGCTGTTATTTTCTTTTATCTTAAACAATATTTTTGATTAGCTGGAA 1200  
AAAAAGTAAAGTGTGCAATAAAGAAATAAGAAATGTTATAAAAAATAATCGACCTT

a b c  
P F I S Q L L F S P I L T I F P F D \* L E -  
F S F H S C Y F L L S \* Q Y F L I S W K -  
F H F T A V I F F Y L N N I F C L A G S -

1201 GTAAAAAGTATCAAAATAGAGAAGCGCTAGACTGAGGTAACCTTAGCTTATTCACATTCAT 1260  
CATTTTTCATAGTTATTCTCTTCGCGATCTGACTCCATTGAATCGAATAAGGTAGAATA

a b c  
V K S I K \* E K R \* T E V T \* L I H I H -  
\* K V S N K R S A R L R \* L S L F T F I -  
K K Y Q I R E A L D C G N L A Y S H S -

1261 AGATCGACCTTCATATATCCAAATACGATGATAAGGAACAGCAGCTATCCGTTTAAAAA 1320  
TCTAGCTGGAAGTATATAGTTATGCTACTATTCCTTTGTCGTCAGTAGGCAAAATTTTT

a b c  
R S T F I Y P I R C \* G N S S H P F \* K -  
D R P S Y I Q Y D D K E T A V I R F K N -  
I D L H I S N T M I R K Q Q S S V L K I -

1321 TAGTGCTATGAGGACTAAATTTTATAGAGTCAAGAAATGGAAGCGAAATCTTAATCAAAAA 1380  
ATCACGATACCTCGATTAAAAAATCTCAGTCTTTTACCTCGGCTTTAGAAATAGTTTTT

a b c  
\* C Y E D \* I F R V K K K W S R N L N Q K -  
S A M R T K F L E S R N G A E I L I K K -  
V L C G L N F \* S Q E M E P K S \* S K R -

1381 GAATTGCGTCGATATGCAAAAGAAATCGAACTCTAAATCTTTGCTTAAATAGATTACCA 1440  
CTTAACGCAGCTATAACGTTTCTTAGCTTGAGATTAGAAAGCAATTATTCATAATGCT

a b c  
E L R R Y C K R I E L \* I F R \* V L P -  
N C V D I A K E S N S K S F V N K Y Y Q -  
I A S I L Q K N R T L N L S L I S I T N -

1441 ATCTTGATTGATTGAAGAGATTGACGAGGCAACTGCACAGAAATCATTAAGAAATAAA 1500  
TAGAACTAACTAACTCTCTAACTCGCTGACGTCCTCTAGTAAATTTCTTTATTT

a b c  
I L I D C R D \* R G N C T E D H \* R N K -  
S C L A E I D E A T A Q K I I K E I K -  
L D C L K R L T R Q L H R R S L K K \* S -

1501 GTAACCTTTTATTATAGAGAATAAATAAATACTAATAATAGAGATCAGCGATCTTCAA 1560  
CATTGAAAAATAATTAATCTCTTATTGATTAAATGATTATCTCTAGTCGCTAGAAGTT

a b c  
V T F I N \* R I N \* I T N I E I S D L Q -  
\* L L L I R E \* T K L L I \* R S A I F N -  
N F Y \* L E N K L N Y \* Y R D Q R S I -

1561 TTGACGAAATAAAGCTGAAGTAAAGTTAGACAATAAAAAATACAAACCTGGTCAAAAT 1620  
AAGTCTTTATTTTCAGCTGATTTCAATCTGTTATTTTATGTTTGAACACAGTTTAT

a b c  
L T K \* K L N \* S \* T I K N T N L G Q N -  
C R N K S C T K V R Q \* K I Q T L V K I -  
D E I K A E L K L D N K K K Y K P W S K Y -

1621 ATTGAGGAAGAAAGAGACCGTTAGCAAAAGAAATAAGGCAATAAATAAATGA 1680  
TAACCTCTCTCTTCTTCTGCTCAATCTGTTCTTTCTTTTATTCCTGTTATTTTATTCT

a b c  
I E G K E D Q L A K E K I R Q \* I K C -  
L R K E K K T S \* Q K K K \* G N K \* N E -  
C G R K R R P V S K R K N K A I N K H S -

FIGURE 12 (cont.)

1681 GTACAGAAAGTGAAGAAATAAAAGATTTATTTTTTTCATTAATTTATTGAAAGAGGGGTT 1740  
 CATGTCTTCACTTCTTTATTTTCTAAATAAAAAAGTTATTAATAACTTTTCTCCCCAA

a V Q K C R N K R F I F F N N L L K R G V -  
 b Y R S E E I K D L F F S I I Y C K E G F -  
 c T E V K K \* K I Y F F Q \* F I E K R G F -

1741 TTGGGGTTTTGGGGTTTTGGGG 1762  
 AACCCEAAACCCCAAAACCCC

a L G F W G F G -  
 b W G F G V L G -  
 c G V L G F W -

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FIGURE 14

132 LSTQKQYFQDEMNQVRAMIGNEL.FRHLYTKYLIFORTSE...GTLVQFC 178  
 1 MSRRNQ.....KKQAP.PIGNETNLDVQLNLEVYKQIEHYTKQOQOI 43  
 179 GNNVFDHLKVNDKFKKQGGGAADNPEACCSTCKYMNQEKDHFPLNIN 228  
 44 KEEDLKLLKFQNDQDQNGSNDODDEE.....MNSNKQELLRRVN 84  
 229 VPMNRNMKSRTIFVYCTHFRNRNQFFKHIEFVSNOMNISAMDRAQITFN 278  
 85 .....QIKQOVQLIKK...VGSKEVDLNLNEDENKKN 114  
 279 IFRFNRIKLLKDVIEKIAHYLKVVDNFNNYTYTKSCPLPMWRERKQ 328  
 115 GLSEQQVKEQLATITEQVKYQNLVFNMDVQLDLNESGGHRRHRETDY 164  
 329 KIENLINKTREETSKYEELESYTTDNKCVTOFINE.FFYNILKFOPLTG 377  
 165 DTEKMF.EISHDQ.....NYVSIYANQKTSYCWMLKDYFNK 200  
 378 RNRKNFQKXVKYVELNKHLELHKNLLEKINTREISWQVETSASHFY 427  
 201 NNYGNLNVSDMLLE...TEAFYAFDDPSQTIKLTNNSYQTVNID..... 242  
 428 FDHENIYVLWKLRLWI...PEDLVSLIRCFYFYTEQKSYSTKYTYRKN 451  
 243 VNFDMNLCLALLRPLUSDLPNILNRSY...TRNQYNEKIGELLETI 290  
 476 WDVIMHMSIADLKETLAEVQEKVEEWCKSLGFAPGKRLIFPKTTFFP 525  
 291 FAVVFSHR.....HLQGHQVCEAFQYLVNSSQISVKDSQ 330  
 526 IMTFNKKIVNSDRKTTKLTNTKLLNSHLMKTLKQRMFKDPPGFVFN 575  
 331 VYSFSTDLKVD...TNKVQDYFKLQEFRLTHVSQAIPVSATNAVENL 378  
 576 DDVMKYEFEVCKMKQVGGPKLP.....FATMDIEKCYDS...VNREK 615  
 379 NVLLKKVRH...ANLNVSIPTQFNEDFYFVNLQHLKLEFGLFNLTKQK 426  
 616 LSTFL.....XTKLLSSDFWINTAQILKKNNI...VIDSKNFRKKEMK 657  
 427 LENLLSIKQSGKLFRLNFYTYVAQETSRQILQATTIKGLKNNKQ 476  
 558 DYFRQKFKIALEGQYPTLPSVLEN...EQNDLNAKKTLLIVEAKQRYFK 705  
 477 EETPETKDETPESTSGMKFFDHLSELTELEDFSVN...LQATQEIY... 520  
 706 KDNELQPVNICQYNYINFNGKFKYQTKGIPQGLCVSSILSSFFYATLEE 755  
 521 .DSLHKLIRSTNLKFKLSYKYENEKSKMDTFIDLKNI...YETLNN 564  
 756 SSLGFLRDESHNPNPNVNLMLRLTDDYLLITTOENNAVLPIEKLINVSR 805  
 565 .....LKRCVSINSHPHGNISYELTN.....KDSYFKKLTNGE 600  
 806 ENGKFNMKLQTSFPLSPSKFAKYGMSVEEQNIQDYCDWIGISIDMK 855  
 601 LQHAAYFK...QNEQFNKNSAKIESSESLESDIDSLCKSASCKNLQ 648  
 856 TLALMPNINLRIEGLICTLNLNMOT...KASMWLKK...KLKSFLONNITH 901  
 649 NVNI.....IASLLYNNIQGNPFNKNLLFFKQFELKLNENVSINC 691  
 902 YFRKTI...TTEDFANKTLANKLISGGYKYMCAKEYKDHFKKNLMSM 948  
 692 ILDQHILNSISEFLEKNKKIKAFILKRYLLQYLYDYTKLFTLOQLPEL 741  
 949 IDLEVSRIIYSVT.....RAFFKYLVNCKIDT...IFGEEHY 982  
 742 NOVYINQOLEELTVSEVHKQVWENHKQKAFYEPCEFIKESSTQLQIDF 791  
 793 PDDFLS...TLKHPIEIFSTKKYIFNRVCMILKAELKSDOCOSILQ 1028  
 792 DQNTVSDDSIKKILESISESKYHYHRLNLSQSSSLIKSENEETQELK 840

FIGURE 15

4 DIDDDIENLNTFTFKYSSSSCDKKGCKTLKSGSKSPSLTPK..... 47  
617 NVKSAKIESSSLESLEDISLCSIASCNQNLQNNVIAISLLYPNNIKQP 666  
48 .....LQKLEFYFSDANLYNDSFRRLVLKSGEQRVE.....IETLLM 86  
667 FNKPNLFFKQFQOLKNLNVINCILDQHLINISIEFLEKNKIKAPIL 716

**CONCLUSIONS**

FIGURE 16

```

1 MENDIDLDDIENL.....LPNTFNKYSSSCSDKKGCKTLKSGSKSPS... 42
  : : : : : : : : : : : : : : : : : : : : : : : : : : : :
491 IELAIAVNNLDEIKGHTAIFSDVSGSMSTSMGGAKKYGSVRTCLEC 540
  : : : : : : : : : : : : : : : : : : : : : : : : : : : :
43 .LTIPKLQKQ .....LEFYFSDANLYNDSFLRLKLVLKSGEQRVEIETLL 85
  : : : : : : : : : : : : : : : : : : : : : : : : : : : :
541 ALVLGLMVKQRCEKSSFYIFSPPSSQCNCYL .EVDLPGDELRPMSQKLL 589
  : : : : : : : : : : : : : : : : : : : : : : : : : : : :

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FIGURE 17

	Motif A	Motif B
Consensus	h-h <h1>h</h1> -h-h-h	h----- <h1>Q</h1> --sp
telomerase p123	KQRNLHCTVATDIEKYSYVPSREKLSTFLTKTLL-100-RFYKQTGIP <h1>D</h1> CUCVSLSLSSFYATLESSLGLP <h1>L</h1>	
Dong (LINE)	GKNRLHCTVATDYAKAFDSIPHSMLIOVLVEIKIN-28-ROIAIKGTGYQEDSIS?MFCULANPLSHQLHNDR	
al S.c.(group I)	KGRNLRPRELVKKCFDTSLHDLLIKELERYISD-26-HVPEGVPRVCVCGAPSPALCANVALRLOERLAGLA	
HIV-RT	VPGGSNWTFRELVKKCFDTSLHDLLIKELERYISD-7-GTRYQNVVLCPWCKESPAIFQSMMTKILFFPKRON	
L8543_12 y <sup>m14</sup>	LKKKSVTVLIDVGDAITSVLPDEDFRKTYATPIK-68-KCIYEEDGLGFQESSLSA?IVDLVYDDLLLFYSEFK	
	VLPELYTKCFDVKSYDSIPRMECMRIKDKALKN-	
	Motif C	Motif D
Consensus	h-y <h1>R</h1> DDhh	Ch-h---K
telomerase p123	-14-LMRITDDVLTATTTOENN-0-AVLFIKLIINVSRNGFKNFRLOT-23-QDYCVLGEGISI	h-hlgch-h
Dong (LINE)	-16-LHLYMDIKYAVKDKE-0-MKKLIDITTTFSNDLSMQFLIKET-25-KC-VKYVLEGQQ	
al S.c.(group II)	-55-YVRVAENLIIVLGSKN-2-KIIRDKANFNLS LGTINEERKLI-4-ETPARFICNI	
HIV-RT	-4-IYQMDLVYGHGLEIG-1-HRTKTELRQHLLKGLTPDRKOK-0-BEPFLMGVEL	
L8543_12 y <sup>m14</sup>	-8-ILKADVDLLISTDQQ.....VINIKLMGCEQKYNRR-41-FRSKSGCIFR	

FIGURE 18

telomerase p43	LQKQIEFYESDANLYNDSEFLRKLVLKSGEQRVEIETLLM
human La	ICHQIEFYEGDENLPRDRFLKEQI.KLDEGWVPLEIMIK
Xenopus LaA	ICEQIEFYEGDENLPRDRFLKQOI.LLDDGWVPLETMIK
Drosophila La	ILROVEFYEGDANLNRRDRFLREQIGKNEDGWVPLSVLVT
S. c. Lhp1p	CLKQIEFYSEENFFPYDRFLRTTAEK.NDGWVPISITAT

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FIGURE 19

1 aactcatta attactaatt taatcaacaa gattgataaa aagcagtaaa taaaacccaa  
61 tagatttaatt ttagaaga tcaattgaaa aatggaaatt gaaacaact aagcacataa  
121 gccaaaagcc gaaaaattgt ggtgggaact tgaattagag atgcaagaaa accnaaatga  
181 tataatagtt aggggttaaga ttgacgatcc taagcaatat ctctggaacg tcaatcgacg  
241 atgtttgttg taggaaggtta gttactacta agataaagat gaaagaagat atatcatcac  
301 taaagcactt ctgaggtgg ctgagictga tctgagttc atctgctagt tggcagctta  
361 catccgtaat gaactttaca tcagaactac cactaactac atttagcat tttgtgtgt  
421 ccacaagaat actcaacct tcatcgaaa gtacttcaac aaagcagtag tttgcttaa  
481 tgacttactg gaagttctg aatttgcata ggttctctat attttgatg caactgaatt  
541 caaaaatttg tatctgata ggatacttct ataagatat ctgaaggac tcactttccg  
601 taagtgttta caaagatgctg tcagaagcaa gttttctgaa ttcaacgaat actaacttgg  
661 taagtattgc actgaatcct aacgtaagaa aacaattgtc cgttacctct cagtaccaa  
721 caagtaaaag tgggattaaa ctaagaagaa gagaaaagag aatctcttaa ccaacttta  
781 ggcaataaag gaacttgaag ataagtcmaa gagagaactt ggagacataa tgaactgtga  
841 agatgaactc aaggctttaa aaccagcagt tatgaagaaa atagccaaga gatagaatgc  
901 catgaagaaa cacatgaagg cacttaaaat tcttaactct accttgaat caaagtactt  
961 gacettcaag gatctcatta agttctgcca tattctgag cctaaagaaa gagtctataa  
1021 gatccttggg aaaaaatacc ctaagaccga agaggaatac aaagcagcct ttggtgttcc  
1081 tgcactgcca cccctcaatc ctgaattggc tggaaagcgt atgaagatg aaactcttaa  
1141 aacatgggaa aatgaactca gtgcaaaagg caacactgct gagettgtgg ataatttaatt  
1201 ttcaagcaat taactcccat atatggccat gttacgtaac ttgtctaaca tcttaaaagc  
1261 cgggttttca gatactacac actctattgt gatcaacaag attgtgagc ccaagccgct  
1321 tgagaactcc aagatgttcc ctctcaatt ctttagtgcc attgaagctg ttaatgaagc  
1381 agttactaag ggaattcaagg ccaagaagag agaaaaatag aatctaaag gtcaaatcga  
1441 agcagtaaaag gaagttgttg aaaaaaccga tgaagagaag aaagatatgg agttggagta  
1501 aaccgaagaa ggagaatttg ttaaaagtaa cgaagggaatt ggcaagcaat acattaaact  
1561 catgaactt gcaatcaaga tagcagttaa caagaattta gatgaataca aaggacacac  
1621 tgcaatcttc tctgatgitt ctggttctat gagtacctca atgtcaggtg gagccaagaa  
1681 gtatggttcc gtctgacttt gtctcgagtg tgcattagtc ctggtttga tggtaaaata  
1741 acgtttgaa aagtcctcat tctatcttct cagttcacct agtttcaat gcaataagtg  
1801 ttacttgaag gtgatctcc ctggagacga actccgtctc tctatgtaa aacttttga  
1861 agagaaaagga aaacttgggt gtgttactga ttccctcat gagtgcattg atgaatgacg  
1921 aaagaataaa atcacgtag acaattatgt tattttgtct gatgatgta tgcagaagg  
1981 atattcagat atcaattgta gaggcagttc cattgttaac agcatcaaaa agtacaagga  
2041 tgaagttaaa cctaacttta aaacttttgc agttgactta gaaggtttag gaaagtgcct  
2101 taatctaggt gatgagtica atgaaaacaa ctacatcaag atattcggtta tgaagcattc  
2161 aatcttaaag ttactttcag ccaagcaagg aggagcaaat atgttcgaag ttatcaaaa  
2221 ctttgccttc caaaaatag gacaaaagt agtttctga gattcttcta taacaaaat  
2281 ctaccccac tttttgtt tattgcatag ccaattatga atttaatta ttactatt  
2341 atttaagtta cttactagt ttatgtatcg cagtctatta gctactcaa atgattctgc  
2401 aaagaacaaa aaagattaaa a

FIGURE 20

MEIENNQAQQPKAEKLWWELEMQENQNDIQVRVKIDDPKQYL  
VNVTAACLLQEGSYQDKDERRYIITKALLEVAESDPEFICQLAVYIRNELYIRTTTN  
YIVAFVCVVHKNTQPFIEKYFNKAVLLPNDLLEVCEFAQVL YIFDATEFKNLYLDRILS  
QDIRKELTFRKCLQRCVRSKFSEFNEYQLGKYCTESQRKKTMFRYLSVTNKQKWDQTK  
KKRKENLLTKLQAIKESEDKSKRETGDIMNVEDAIKALPAVMKKIAKRQNAMKKHKMK  
APKIPNSTLESKYLTFKDLIKCHISEPKERVYKILGKKYPKTEEEYKAAFSDSASAP  
FNPELAGKRMKIEISKTWENELSAKGNTAEVWDNLISSNQLPYMAMLRNLSNILKAGV  
SDTTHSIVINKICEPKAVENSKMFPLQFFSAIEAVNEAVTKGFKAKKRENMNKKGQIE  
AVKEVVEKTDEEKKDMELEQTEEGEFVKVNEGIGKQYINSIELAIKIAVNKNLDEIKG  
HTAIFSDVSGSMSTSMGGAKKYGSVRTCLECALVLGLMVQRCESFYIFSSPSSQ  
CNKCYLEVLDLPGDELRPMSQKLLQEKGLGGGTDFFPYECIDEWTKNTHVDNIVILSD  
MMIAEGYS DINVRGSSIVNSIKKYKDEVNPNIKIFAVDLEGYGKCLNLGDEFNENNYI  
KIFGMSDSILKFISAKQGGANMVEVIKNFALQKIGQK

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FIGURE 21

1 tcaatactat taattaataa ataaaaaaa gcaactaca aagaaatgt caaggcgtaa  
61 ctaaaaaag ccataggctc ctataggcaa tgaacaaat ctgtatttg taftacaaaa  
121 tctagaagt tacaaaagcc agattgagca ttataagacc tagtaglaat agatcaaaaga  
181 ggaggatctc aagctittaa agttcaaaaa ttaagattag gatggaaact ctggcaacga  
241 tgatgatgat gaagaaaca actcaataaa ataataagaa ttataagga gagtcaatta  
301 gattaagtag caagtttaat tgataaaaaa agttgtctt aagtgataga aagatttgaa  
361 ttgaaacgaa gatgaaaaca aaaagaatgg actttctgaa tagcaagtga aagaagagta  
421 attaagaacg attactgaag aatagggttaa gtattaaaa ttatatttta acatggacta  
481 ccagttagat taaatgaga gtgggtggcca tagaagacac agaagagaaa cagattatga  
541 tactgaaaaa tgggttgaaa tatctatga ccaaaaaat tatgtatcaa ttacgccaa  
601 ctaaaagaca tcatattgtt ggtggcttaa agattatttt aataaaaaa attatgatca  
661 tctaatgta agcattaaca gactagaaac tgaagccgaa ttctatgcct ttgatgattt  
721 ttcaacaaca atcaaaacta ctaataatc ttactagact gttaacatag acgttaattt  
781 tgataataat ctctgtatc tcgcatgtct tagattttta ttactactag aaagattcaa  
841 tatttgaat ataagatctt ctatcacaag aaattaatat aatttgaga aaattgggta  
901 gctactgaa actacttgc cagttgtctt ttctcatgc cactacaag gcattcattt  
961 acaagttcct tgcgaagcgt tctaatttt agttaactcc tcatcataaa ttacggttaa  
1021 agatagctaa ttataggtat actcttctc tacagactta aaattatgtt acactaaca  
1081 agtccaagat tattttaagt tctataaga attccctcgt ttgactcatg taagctagta  
1141 ggctatccca gttagtgcta ctaacgtctg agagaacctc aatgtttac ttaaaaaggt  
1201 caagcatgct aatcttaatt tagtttctat cctactctaa ttaacttttg atttctactt  
1261 tgttaattta taactattga aattagagtt tggattgaa ccaaatattt tgacaaaaca  
1321 aaagcttgaa aatctacttt tgagtataaa ataactaaaa aatcttaaat ttttaagatt  
1381 aaactttac actcagtggt cttaagaac ctcagaaaaa cagatattaa aacaagctac  
1441 aacaatcaaa aatctcaaaa acaataaaaa tcaagaagaa actcctgaaa ctaagatga  
1501 aactccaagc gaaagcacia gtgggtatgaa atttttgat catctctctg aattaaccga  
1561 gttgaagat ttcagogtta acttgtaagc taccacaaga attatgata gcttgacaaa  
1621 acttttgatt agatcaacaa atttaagaa gttaaaatta agtlacaat attgaatgga  
1681 aaagagtaaa atggatcatc tcatagatct taagaataat tatgaacct taacaactct  
1741 taaaagatgc tctgttaata tatcaaatcc tcatggaac atttctatg aacigacaaa  
1801 taaagatct acttttata aatttaagct gaccttaac taagaattat aacacgttaa  
1861 gtatctttt aagtagaacg aattttaatt taataacgtt aaaagtgc aaattgaaat  
1921 ttccatatta gaaagcttag aagatattga tagtcttgc aaactatgt cttctgtaa  
1981 aaatttaca aaattgtaata ttatgcgcag ttgtctat cccaacata ttagaanaa  
2041 tctttcaat aagcccaact ttctatttt caagcaattt gaataattga aaaatttgga  
2101 aatgtatct atcaactgta ttctgatca gcatatactt aatctattt cagaattctt  
2161 agaaaaaat aaaaaataaa aagcatcatc ttgaaaaga tatttttat tacaatttta  
2221 tcttgattat actaaattat ttaaaacact tcaatagta cctgaattaa aattgattt  
2281 cattaattag caattagaag aattgactgt gagtgaagta cataagtaag tatgggaaa  
2341 ccacaagcaa aaagctttct atgaaccatt atgtagttt atcaagaat catcctaacc  
2401 ccttagcta atagattttg accaaaacac tgtaagtgat gactctatta aaagatttt  
2461 agaacttata tctgactcta agtatcaica ttatttgaga ttgaacctta gtaattctag  
2521 cagtttaatt aaatctgaaa acgaagaat ttaagaactt ctcaagctt gcgacgaaa  
2581 aggtgtttta gtaaaagcat actataaatt cctctatgt ttaccaactg gtacttata  
2641 cgattacaat tcagatagat ggtgattaat taaattatg tttaataaa tattaatat  
2701 tgaatattc ttgtctatt attgataaa tacatacaat agtcatttt agtgtttga  
2761 atattattta gtaatttaatt tcaattttt aagtaataa tatatttca atcattttt  
2821 aaaaaatcg

FIGURE 22

MSRRNQKKPQAPIGNETNLD FVLQNLEVYKSQIEHYKTQQQIK  
EEDLKLLKFKNQDQDGN SGND DDEENNSNKQQELLRRVNQIKQQVQLIKVGSKVEK  
DLNLNEDENKKNGLSEQQVKEEQLRTITEEQVKYQNLVFNMDYQLDNESGGHRRHRR  
ETDYDTEKWEISHDQKNYVSIYANQKTSYCWWLKDYFNKNNDHLNVSINRLETEAE  
FYAFDDFSQTIKLTNNSYQTVNIDVNFDDNNLCILALLRFLLSLRFNILNIRSSYTRN  
QYNFEKIGELLETIFAVVFSHRHLQGIHLQVPCEAFQYLVNSSSQISVKDSQLQVYSF  
STDCLKVDTNKVQDYFKFLQEFPRLTHVSQQAIPVSATNAVENLNVLLKKVKHANLNL  
VSIPTQFNDFYFVNLQHLKLEFGLPNILTKQKLENLLSIKQSKNLKFLRLNFYTY  
VAQETSRKQILKQATTIKNLKNNKNEETPETKDETPSESTSGMKFFDHLSELTELED  
FSVNLQATQEIYDSLHKKLLIRSTNLKKFKLSYKYEMEKSKMDTFIDLKNIYETLNNLK  
RCSVNISNPHGNISYELTNKDSTFYKFKLTNLQELQHAKYTFKQNEFQFN NVKS AKIE  
SSSLESLEDIDSLCKSIASCKNLQNVNIIASLLYPNNIQKNPFNKP NLLFFKQFEQLK  
NLENVSINCILDQHILNSISEFLEKNKKIKAFILKRYLLQYYLDYTKLFTLQQLPE  
LNQVYINQQLEELTVSEVHKQVWENHKQKAFYEPLCEFIKESSQTLQLIDFDQNTVSD  
DSIKKILESISESKYHHYLRNLNPSQSSSLIKSENEEIQELLKACDEKGVLVKAYYKFP  
LCLPTGTYDYNSDRW

FIGURE 23

MKILFEFIQDKLDIDLQTNSTYKENLKC GFHFNGLDEILTTCFAL  
PNSRKIALPCLPGDLSHKAVIDHCHYLLTGELYNNVLTFGYKIARNEDVNNSLFCHS  
ANVNVTLKGAAWKMFHSLVGTAFVDLLINYTVIQFNGQFFTQIVGNRCNEPHLPPK  
WVQRSSSSSATAAQIKQLEPVTNKQFLHKLNNSSFFPYSKILPSSSSIKKLTDLR  
EAIFPTNLVKIPQRLKVRJNLTLQKLLKRHKRLNYVSILNSICPPLEGTVDLSHLR  
QSPKERVLKFHIVILQKLLPQEMFGSKKNKGKIKNLNLLSLPLNGYLPFDSLLKKL  
RLKDFRWLFISDIWFTKHNFNENLQLAICFISWLFRLQIPKIIQTFYCYEISSTVTI  
VYFRHDTWNKLITPFIVEYFKTYLVENNVCRNHNSYTLNHNHSMRIIPKKSNNEFR  
IIAIPCRGADEEEFTYKENHKNAIQPTQKILEYLRNKRPTSFTKIYSPTQIADRIKE  
FKQRLKKFNNVLPelyfMKFDVKSCYDSIPRMECMRILKDALKNENGFFVRSQYFFN  
TNTGVLLKFNVNNASRVPKPYELYIDNVRTVHLSNQDVINVVEMEIFKTALWVEDKCY  
IREDGLFQSSLSAPIVDLVYDDLLEFYSEFKASPSQDTLILKLADDFLIISTDQQV  
INIKKLAMGGFKYNANARDKILAVSSQSDDDTVIQCAMHIFVKELEVWKHSSTMN  
NFHIRSKSSKGIFRSLIALFNTRISYKTIDTNLNSTNTVLMQIDHVVKNISECYKSAF  
KDLSINVTQNMQFHSFLQRIIEMTVSGCPITKCDPLIEYEVRFILNGFLESLSNNTS  
KFKDNIILLRKEIQHLQAYIYIYIHVN

FIGURE 24

*Oxytricha*  
*Euplotes*

LCVSYILSSFYYANLEENALQFLRKESMDPEKPETNLLMRLT  
LCVSSILSSFYYATLEESLGFLRDESMNPENPNVNLLMRLT

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FIGURE 25

Motif 0

human AKFLHMLMSVYVVELLRSPFYVTETTFQKNR  
 tez1 ISEIENLVLGKRSNAMCLSDFEKRRQIFAEFIYWLNSFIIPILQSFYITESSDLNR  
 EST2 LKDFRWLFISD---IWFTKHNFENLNQLAICFISWLPRLQIPKIIQTFFCYTEISSTVT-  
 p123 TREISHMQVET-SAKHFIYFDHEN-IYVLWKLRLWIFEDLVVSLIRCFYVVEQQKSYSK

..\*.....\*\*

Motif 1

human LFFYRKSVHSLQSIGIRQHLKRVQLRDVSEAEVRQHRARPALLTSRLRFIPKP--DGL  
 tez1 TVYFRKDIWKLRCRFFI-TSMKMEAFKINENNVRMDTQK-TTLPPAVIRLLPKK--WTF  
 EST2 IVYFRHDTWNKLITPFIYEFKTYLVENNVCRNHNSTLS--NFNHSKMRIIPKKSNEF  
 p123 TYYYRKNIWDVIMKHSI-ADLKKETLAEVQKEVEEWKKS-LGFAPGKLRLLPKK--TTF

...\*.\*.\*.\*.\*.\*.\*.\*.\*.\*

Motif 2

human RPIVNMDYVVGARTFRREKRAERLTSRVKALF-SVLNYERA  
 tez1 RLITN-LRKRFLIKMGSNNKMLVSTNQTLRPVASILKHLINESGIPFNLEVYMKLLTF  
 EST2 RIITAIPCRGADEEFTIYKENHKNAIQPTQKILEYLRNKRPTSTFKIYSTQIADRIKEF  
 p123 RPIMTFNKKIVNSDRKTTKLTNTKLLNSHMLKLTKN-RMFKDPPGPAVFNVDVMMKY

\*.\*.\*.\*.\*.\*.\*.\*.\*.\*

Motif 3 (A)

tez1 KKDLLKHRMGR-KKYFVRIDIKSCYDRIKQDLAFRIVKK-KLKDPEFVIRKYATIHTS  
 EST2 KQRLKKFNNVLPelyPMKFDVKS CYDSIPRMECHRILKD-ALKNENGFFVRSQYFFNTN  
 p123 EEFVCKWKQVGPQLFPATMDIEKCYDSVNRKLSFLKTTKLLSSDFWIMTAQILKRNK

\*.\*.\*.\*.\*.\*.\*.\*.\*.\*

2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022 2023 2024 2025 2026 2027 2028 2029 2030 2031 2032 2033 2034 2035 2036 2037 2038 2039 2040 2041 2042 2043 2044 2045 2046 2047 2048 2049 2050 2051 2052 2053 2054 2055 2056 2057 2058 2059 2060 2061 2062 2063 2064 2065 2066 2067 2068 2069 2070 2071 2072 2073 2074 2075 2076 2077 2078 2079 2080 2081 2082 2083 2084 2085 2086 2087 2088 2089 2090 2091 2092 2093 2094 2095 2096 2097 2098 2099 2100 2101 2102 2103 2104 2105 2106 2107 2108 2109 2110 2111 2112 2113 2114 2115 2116 2117 2118 2119 2120 2121 2122 2123 2124 2125 2126 2127 2128 2129 2130 2131 2132 2133 2134 2135 2136 2137 2138 2139 2140 2141 2142 2143 2144 2145 2146 2147 2148 2149 2150 2151 2152 2153 2154 2155 2156 2157 2158 2159 2160 2161 2162 2163 2164 2165 2166 2167 2168 2169 2170 2171 2172 2173 2174 2175 2176 2177 2178 2179 2180 2181 2182 2183 2184 2185 2186 2187 2188 2189 2190 2191 2192 2193 2194 2195 2196 2197 2198 2199 2200 2201 2202 2203 2204 2205 2206 2207 2208 2209 2210 2211 2212 2213 2214 2215 2216 2217 2218 2219 2220 2221 2222 2223 2224 2225 2226 2227 2228 2229 2230 2231 2232 2233 2234 2235 2236 2237 2238 2239 2240 2241 2242 2243 2244 2245 2246 2247 2248 2249 2250 2251 2252 2253 2254 2255 2256 2257 2258 2259 2260 2261 2262 2263 2264 2265 2266 2267 2268 2269 2270 2271 2272 2273 2274 2275 2276 2277 2278 2279 2280 2281 2282 2283 2284 2285 2286 2287 2288 2289 2290 2291 2292 2293 2294 2295 2296 2297 2298 2299 2300 2301 2302 2303 2304 2305 2306 2307 2308 2309 2310 2311 2312 2313 2314 2315 2316 2317 2318 2319 2320 2321 2322 2323 2324 2325 2326 2327 2328 2329 2330 2331 2332 2333 2334 2335 2336 2337 2338 2339 2340 2341 2342 2343 2344 2345 2346 2347 2348 2349 2350 2351 2352 2353 2354 2355 2356 2357 2358 2359 2360 2361 2362 2363 2364 2365 2366 2367 2368 2369 2370 2371 2372 2373 2374 2375 2376 2377 2378 2379 2380 2381 2382 2383 2384 2385 2386 2387 2388 2389 2390 2391 2392 2393 2394 2395 2396 2397 2398 2399 2400 2401 2402 2403 2404 2405 2406 2407 2408 2409 2410 2411 2412 2413 2414 2415 2416 2417 2418 2419 2420 2421 2422 2423 2424 2425 2426 2427 2428 2429 2430 2431 2432 2433 2434 2435 2436 2437 2438 2439 2440 2441 2442 2443 2444 2445 2446 2447 2448 2449 2450 2451 2452 2453 2454 2455 2456 2457 2458 2459 2460 2461 2462 2463 2464 2465 2466 2467 2468 2469 2470 2471 2472 2473 2474 2475 2476 2477 2478 2479 2480 2481 2482 2483 2484 2485 2486 2487 2488 2489 2490 2491 2492 2493 2494 2495 2496 2497 2498 2499 2500 2501 2502 2503 2504 2505 2506 2507 2508 2509 2510 2511 2512 2513 2514 2515 2516 2517 2518 2519 2520 2521 2522 2523 2524 2525 2526 2527 2528 2529 2530 2531 2532 2533 2534 2535 2536 2537 2538 2539 2540 2541 2542 2543 2544 2545 2546 2547 2548 2549 2550 2551 2552 2553 2554 2555 2556 2557 2558 2559 2560 2561 2562 2563 2564 2565 2566 2567 2568 2569 2570 2571 2572 2573 2574 2575 2576 2577 2578 2579 2580 2581 2582 2583 2584 2585 2586 2587 2588 2589 2590 2591 2592 2593 2594 2595 2596 2597 2598 2599 2600 2601 2602 2603 2604 2605 2606 2607 2608 2609 2610 2611 2612 2613 2614 2615 2616 2617 2618 2619 2620 2621 2622 2623 2624 2625 2626 2627 2628 2629 2630 2631 2632 2633 2634 2635 2636 2637 2638 2639 2640 2641 2642 2643 2644 2645 2646 2647 2648 2649 2650 2651 2652 2653 2654 2655 2656 2657 2658 2659 2660 2661 2662 2663 2664 2665 2666 2667 2668 2669 2670 2671 2672 2673 2674 2675 2676 2677 2678 2679 2680 2681 2682 2683 2684 2685 2686 2687 2688 2689 2690 2691 2692 2693 2694 2695 2696 2697 2698 2699 2700 2701 2702 2703 2704 2705 2706 2707 2708 2709 2710 2711 2712 2713 2714 2715 2716 2717 2718 2719 2720 2721 2722 2723 2724 2725 2726 2727 2728 2729 2730 2731 2732 2733 2734 2735 2736 2737 2738 2739 2740 2741 2742 2743 2744 2745 2746 2747 2748 2749 2750 2751 2752 2753 2754 2755 2756 2757 2758 2759 2760 2761 2762 2763 2764 2765 2766 2767 2768 2769 2770 2771 2772 2773 2774 2775 2776 2777 2778 2779 2780 2781 2782 2783 2784 2785 2786 2787 2788 2789 2790 2791 2792 2793 2794 2795 2796 2797 2798 2799 2800 2801 2802 2803 2804 2805 2806 2807 2808 2809 2810 2811 2812 2813 2814 2815 2816 2817 2818

**U.S. DEPARTMENT OF AGRICULTURE**

FIGURE 28

GCCAAGTTCTGCACTGGCTGATGAGTGTGTACGTCGTCGAGCTGCTCAGGTC  
TTTCTTTTATGTCACGGAGACCACGTTTCAAAAGAACAGGCTCTTTTCTACC  
GGAAGAGTGTCTGGAGCAAGTTGCAAAGCATTGGAATCAGACAGCACTTGAA  
GAGGGTGCACTGCGGGACGTGTCGGAAGCAGAGGTCAGGCAGCATCGGGA  
AGCCAGGCCCGCCCTGCTGACGTCCAGACTCCGCTTCATCCCCAAGCCTGACG  
GGCTGCGGCCGATTGTGAACATGGACTACGTCGTGGGAGCCAGAACGTTCCG  
CAGAGAAAAGAGGGCCGAGCGTCTCACCTCGAGGGTGAAGGCACTGTTCAGC  
GTGCTCAACTACGAGCGGGCGCG

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FIGURE 29

MTEHHTPKSRILRFLENQYVYLCTLNDYVQLVLRGSPASSYSNICERLRSVDQTSFSIFLHSTVVGF  
 DSKPDEGVQFSSPKCSQSELIANVVKQMFDESERRRNLMMKGFSMNHEDFRAMHVNGVQNDLV  
 STFPNYLISILESKNWQLLEHGS DAMHYLLSKGSFEALPNDNYLQISGIPLFKNNVFEETVSKKRK  
 RTIETSITQNK SARKEVSWNSISIRFSIFYRSSYKKFKQDL YFNLHSICDRNTVHMWLQWIFPRQFG  
 LINAQVVKQLHKVIPLVSQSTVVPKRLLKVYPLIEQTAKRLLHRISLSKVYNHYCPYIDTHDDEKILS  
 YSLKPNQVFAFLRSILVRVFPKLIWGNQRIFEIILKDLETFLKLSRYESFSLHYLMSNIKISEIEWLVL  
 GKRSNAKMCLSDFEKRKQIFAEFIYWL YNSFIIPILQSFFYITESSDLNRRTVYFRKDIWKLLCRPFIT  
 SMKMEAFEKINENNVRMDTQKTTLP PAVIRLLPKKNTFRLITNLRKRFLIKMGSNKKMLVSTNQT  
 LRPVASILKHLIN EESSGIPFNLEVYMKLLTFKKDLLKHRMFGRKKYFVRIDIKSCYDRIKQDLMFR  
 IVKKKLKDPEFVIRKYATI HATSDRATKNFVSEAFSYFDMVPFEKV VQLLSMKTSDTLFDVDFDY  
 WTKSSSEIFKMLKEHLSGHIVKIGNSQYLQKVGIPQGSILSSFLCHFYMEDLIDEYLSFTKKKGSVL  
 LR VDDFLFITVNKKDAKKFLNLSRGFEKHNFSTLEKTVINFENSNGIINNTFFNESKKRMPFFG  
 FSVNMRLDITLLACPKIDEALFNSTSVELTKHMGKSFFYKILRSSLASFAQVFDITHNSKFNSCCNI  
 YRLGYSMCMRAQAYLKRMDIFIPQRMFITDLLNVIGRKIWKKLAEILGYTSRRFLSSAEVKWLFCL  
 LGMRDGLKPSFKYHPCFEQLIYQFQSLTDLIKPLRPVL RQVLF LHRRIAD

00760000-007601

[illegible]

FIGURE 30 (cont.)

ATGgiacgigicgggtctcgagacttcagcaaatatgacacatcagGCTTTTTGTCTTGAATGAGAGATGGTTTGAAACCCCTTT  
TCAAAATATCATCCATGCTTCGAACAGCTAATATACCAATTTTCAGTCATTGACTGATCTTATCAAGCCGC  
TAAGACCAGTTTTGCGACAGGTGTTATTTTTACATAGAAGAAATAGCTGATTAAtgicattttcaattattatatacatcctt  
tattactgggtgiccttaacaatattactaagtagctgacccccaaagcaagcactataggattctagtaaaagtaaaatcctcgttattattgttgacttgicctt  
atccttatacttttaagaaagattgacagtggtgicgactactgcccacatgcccatlaaacgggagtggttaaacattaaaagtaatacagaggctaactcccttcatttag  
aataaggaaagtgggtttctataatgataatgccccgactaagcaaaaagcgaagattatctctaaacaaggggggaatagcatatcgaaaggaaaagagagataat  
accagtggttggaagaagcaaggataattggacaagctctgcagatgacaggctaaatttggtgacggaatttggaagccccaggttatccatgggtggccg  
gacctgctactgagcgaagaagaactaaggatagttgaaatactaatagctcatttaagtcttatataagggtttgtttttccgacttcaattttgcatgggtgaaaaaata  
ggtftaagccattattggattccgaaatagccaaatttctgttctctaaagcgggaagcttaagaacttattgaagcttatgaggttcaaaaactccctctgatttaaggga  
gaactctccacgatgaggaaatggatagcttatcagctgctgagggaagcctaatttttgcaaaaagaaaatacattgggagacatctcttgatgaatcagatgcgga  
gagatctccagcggatccttgatgtcaataacttctattttcgaaatgtatggtctactgtcgttcgacttctcgtactctacgcagtttaagtgaccaaaggatcc

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FIGURE 31

EST2 pep	FFYCTEISST VETIVYFRHDT WN----	KLIT P-----FIVE YFK-TYLVEN	40
Euplotes pep	FFYVTEQQKS YSKYIYYRKN IWDVI-MKMS	IAD----LKK ETLA--EVQE	43
Trans of tetrahymen	-----KHKE GSGIFYRRKP IWKLVSRLTI	VKVRIQFSEK NKQMKNFYQ	44
Consensus	FFY.TE..K. .S..YYRK. IW...-KL..	.....F..K .....V..	50
EST2 pep	NVCRNHNSY- -----	TLNFNHSMKRLTEKSNNE FRITAIPCRG	79
Euplotes pep	KEVEEWKSL -----	-----GFAPGGRRLITPKIT--FRIMTFNKK	78
Trans of tetrahymen	KIQLEENLE KVEEKLIPEL SPQKYPQCKL	RLTEPKGS--FRIMTFLRK	92
Consensus	K...E.....	....F..GRRLTEPK.....FRIMTF.RK	100
EST2 pep	ADEEEFTIYK ENHKNAIQPTQKILEMDRK	RPTSFTKIYS PTQIADRIKE	129
Euplotes pep	IVNSDRKITYK LTNKLLNSHLMLKTLKN	-----RMFK -DPFGFAVFN	120
Trans of tetrahymen	DKQKNIK--- LNLNQILMDSQLVFRNLKD	-----ML-G -QKIGYSVFD	130
Consensus	.....K..K LN.N..L..S QL.L..LN-	-----...IG..VF	150
EST2 pep	FKQRLLMKFN NVL-----	ELLYFMKFD VKSCYD	157
Euplotes pep	YD-DVMKRYE EFCVKWKQVG QPFFATMD	TEKCYD	155
Trans of tetrahymen	NK-QISEKFA QPIEKWQNGK RFLKYVTL-		158
Consensus	.K-...KEF. .F..KWK..G ELKVF.T.D	...CYD	186

0076257 011001

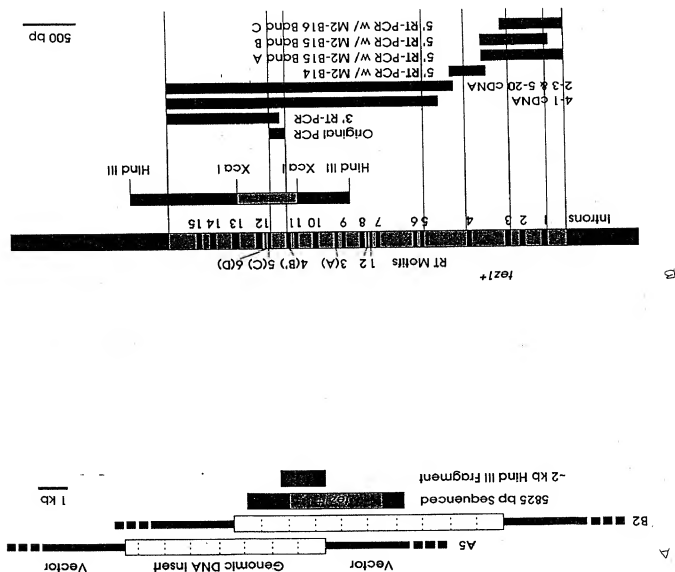
**FIGURE 32**

S-1: FFY VTE TTF QKN RLF FYR KSV WSK  
S-2: RQH LKR VQL RDV SEA EVR QHR EA  
S-3: ART FRR EKR AER LTS RVK ALF SVL NYE

A-1: AKF LHW LMS VYV VEL LRS FFY VTE TTF Q  
A-2: LFF YRK SVW SKL QSI GIR QHL KRV QLR DVS  
A-3: PAL LTS RLR FIP KPD GLR PTV NMD YVV

# COLE

FIGURE 33



0976253-011001

FIGURE 34

Poly 4

	t	a	a	g	t	c	c	t	c	g	
5'-	cag	acc	aaa	gga	att	cca	taa	gg	-3'		
	Q	T	K	G	I	P	Q	G			

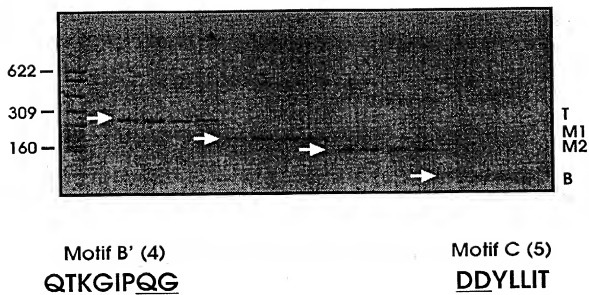
4 (B')

5 (c')

	D	D	Y	L	L	I	T	
3'-	ctg	ctg	atg	gag	gag	tag	tg	-5'
	a	a	a	a	a	a	a	
			t	t		t	t	
					c	c		

Poly 1

FIGURE 35



09756223-011001



FIGURE 36

# PCR Product M2 showed Reasonable Match with Other Telomerase Proteins

```

Ot          LCVSYILSSFYYANLEENALQFLRKESMDPEKPETNLLMRLT
Ea_p123     KGIPQGLCVSSILSSFYYATLEESSLGFLRDESMNPENPNVNLLMRLTDDYLLIT
Sp_M2       SILSSFCHFYMEDLIDEYLSFTKKK-----GSVLLRVV
Sc_p103     DGLFQGSSLSAPIVDLVYDDLLEFYSEFKASPS-----QDTLILKLADDFLIIS
            . * . * . * .
  
```

```

Q K V G I P Q G
Gaa aaa gtt ggt atc cct cag gg..... <---Actual Genomic Sequence.
  
```

## Poly 4

```

      t       c
t a a g c c t c g
gag acc aaa gga att cca taa gg ---->
ag acc aaa gga att cca tca ggC TCA ATT CTG TCA TCT TTT TTG TGT CAT TTC TAT ATG
tc tgg ttt cct taa ggt agt ccG AGT TAA GAC AGT AGA AAA AAC ACA GTA AAG ATA TAC

      K G I P S G S I L S S F L C H F Y M
  
```

```

GAA GAT TTG ATT GAT GAA TAC CTA TCG TTT ACG AAA AAG AAA GGA TCA GTG TTG TTA CGA
CTT CTA AAC TAA CTA CTT ATG GAT AGC AAA TGC TTT TTC TTT CCT AGT CAC AAC AAT GCT

E D L I D E Y L S F T K K K G S V L L R
  
```

```

GTA GTC gac gac tac ctc ctc atc acc
CAT CAG ctg ctg atg gag gag tag tgg
  
```

```

V V D D Y L L I T
  
```

```

<---- ctg ctg atg gag gag tag tgg
      a a a a a a a a
          t t t t
          c c
  
```

## Poly 1

```

.....gac gat ttc ctc ttt ata aca..... <---Actual Genomic Sequence.
      D D F L F I T
  
```

FIGURE 37

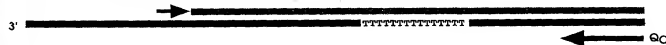
# 3' RT PCR Strategy



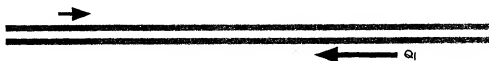
1. Synthesis of cDNA with Q<sub>T</sub> Primer.



2. First Round PCR Using Outside Primer and Q<sub>O</sub> Primer.



3. Second Round PCR Using Inside Primer and Q<sub>I</sub> Primer.



4. Sequence Second Round PCR Products Using Inside Primer or Q<sub>I</sub> Primer.



FIGURE 38

A

-Size Selected Libraries from P. Nurese

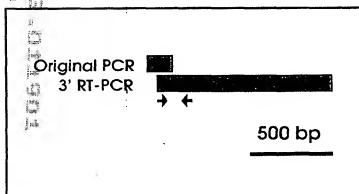
- 3 ~ 4 kb
- 5 ~ 6 kb
- 7 ~ 8 kb
- 11 ~ 12 kb

-Libraries from J.A. Wise  
Sau 3a Partial Digest  
Hind III Partial Digest

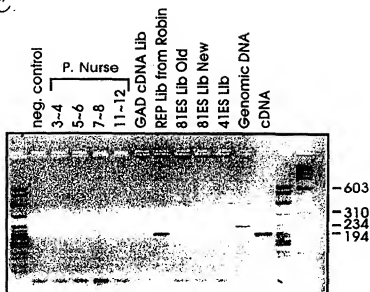
cDNA Libraries

- GAD (Gal Activation Domain) Library
- REP Library from R. Allshire
- REP81ES Library (old)
- REP81ES Library (new)
- REP41ES Library

B



C



D

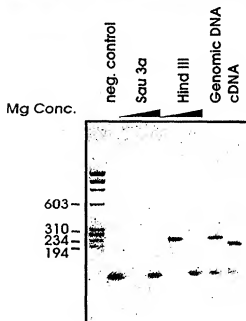
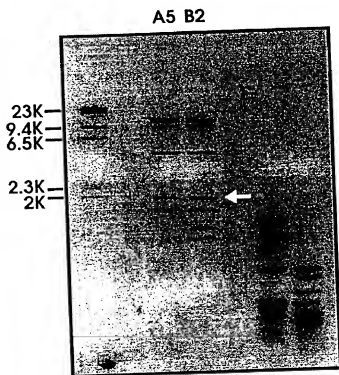


FIGURE 39



Hind III Digested Positive Genomic Clones

FIGURE 40



1. Synthesis of cDNA with Specific Downstream Primer.



2. Ligate Oligo with 5'-P and blocked 3' to cDNA using T4 RNA Ligase.



3. First Round PCR



4. Second Round PCR

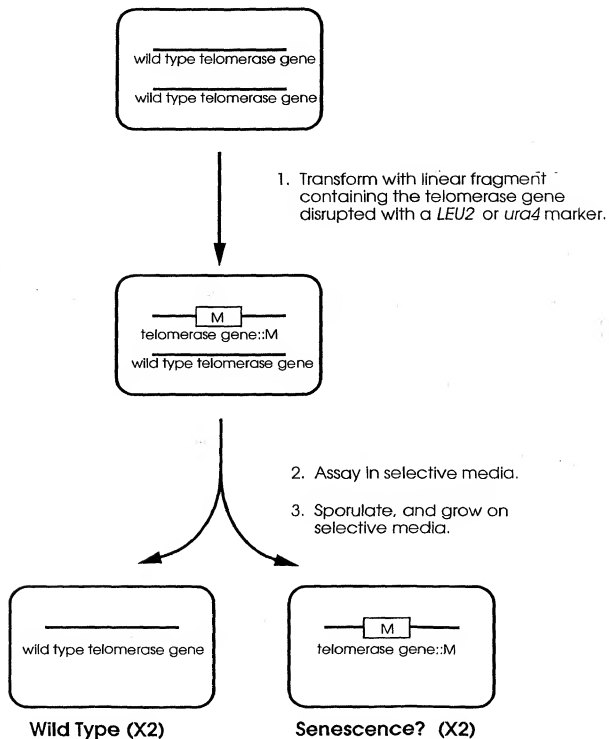






FIGURE 43

Disruption strategy for the putative telomerase genes.



(These cells will show a senescence phenotype if the disrupted gene encodes a telomerase subunit.)



[illegible]

### An Example of Confirmation of *tez1* disruption By PCR

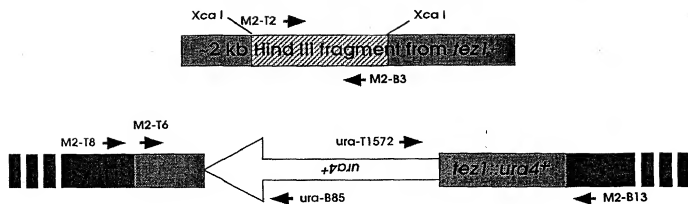
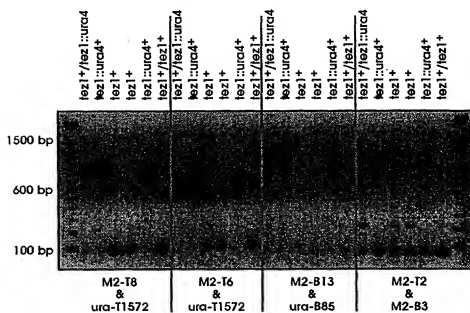


FIGURE 45

*Tez1* disruption causes progressive shortening of telomeres in *S. pombe*

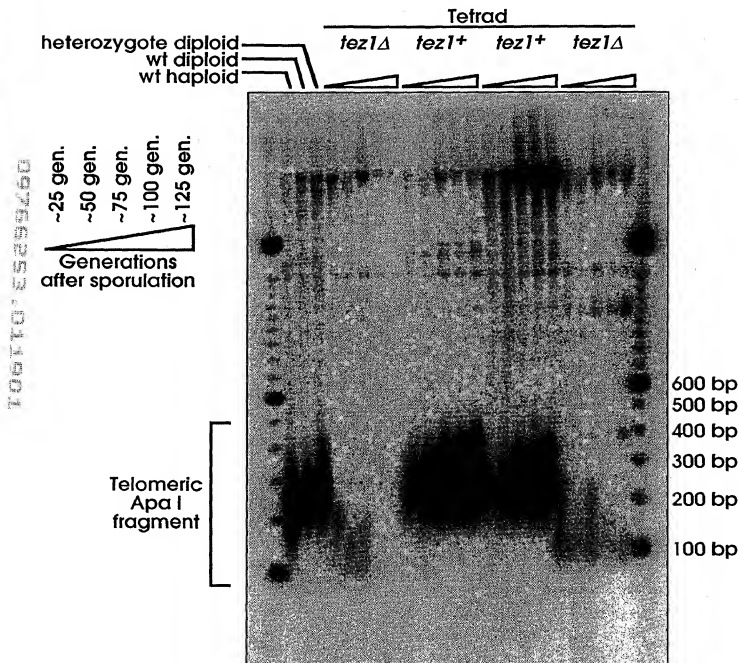


FIGURE 46

1 ggtaccgatttacttttctttctcataagctaattgcttctcgaacgctcctaaatctctggaatatattttacaaga 80  
81 actcaataacaataccaagtcacaaattccaatatgaaggtgttatttagtgatcgataaataatttctattttatcggtcggtta 160  
161 ccaagtataaggacaaaaagaacaacttcttccccctaaagacttttacttttataaatttacttttcaaatataatttcg 240  
241 ggttcgcttactttttaatcgtgggtactgttttagctgctacttctagccaacgcggttttctaccccgctaatgggat 320  
321 agctcttggagtagctcacagaaatccttacaatacttctgatgagactatattagattcattacagtcctgcatattc 400  
401 ttaacatggagccttacacttttagatgagtcacgtcgcatgatggagtatttggatcatccaacgtttgccttgaaaag 480  
481 gttgataattatttgcaaaatcatgtccttagtggtggttaacccggaaggtttttgatgcttgcaacgcttagcatg 560  
561 attgagatattcaaaaatttctatccactacaactcctttaacgcggttttatttttctattttctattctcatgttggt 640  
641 ccaaatatgtatcatctcgtattaggctttttccggttttactcctggaatcgtaaccttttctactattccccctaatga 720  
721 ataactctaaattagtttcgcttataattgatagtagtagaagattgggtgattctactcgtgtaattgttattagtttaa 800  
801 gatactttgcaaaacattttattagctatcattatataaaaaaaatcctataattataaataatcaattatttcggtc 880  
881 actattttttaaacggttatgatcagtaggacactttgcatatataatgttatgcttaatgggttacttgtaacttgc 958

959 ATG ACC GAA CAC CAT ACC CCC AAA AGC AGG ATT CTT CGC TTT CTA GAG AAT CAA TAT GTA 1018  
1 M T E H H T P K S R I L R F L E N Q Y V 20

1019 TAC CTA TGT ACC TTA AAT GAT TAT GTA CAA CTT GTT TTG AGA GGG TCG CCG GCA AGC TCG 1078  
21 Y L C T L N D Y V Q L V L R G S P A S S 40

1079 TAT AGC AAT ATA TGC GAA CGC TTG AGA AGC GAT GTA CAA ACG TCC TTT TCT ATT TTT CTT 1138  
41 Y S N I C E R L R S D V Q T S F S I F L 60

1139 CAT TCG ACT GTA GTC GGC TTC GAC AGT AAG CCA GAT GAA GGT GTT CAA TTT TCT TCT CCA 1198  
61 H S T V V G F D S K P D E G V Q F S S P 80

FIGURE 46 (cont.)

1199	AAA	TGC	TCA	CAG	TCA	GAG	gtatatatat	ttttt	gttttt	gatttttt	ttttt	ctattc	gggatag	ctaata	tatgggcag	1272					
81	K	C	S	Q	S	E										86					
1273	CTA	ATA	GCG	AAT	GTT	GTA	AAA	CAG	ATG	TTC	GAT	GAA	AGT	TTT	GAG	CGT	CGA	AGG	AAT	CTA	1332
87	L	I	A	N	V	V	K	Q	M	F	D	E	S	F	E	R	R	R	N	L	106
1333	CTG	ATG	AAA	GGG	TTT	TCC	ATG	gtaagg	tattcta	aattgt	gaaatatt	tacctg	caattact	gtttc	aaagaga	1405					
107	L	M	K	G	F	S	M									113					
1406	ttgtattta	aaccgataaag	AAT	CAT	GAA	GAT	TTT	CGA	GCC	ATG	CAT	GTA	AAC	GGA	GTA	CAA	AAT	1469			
114				N	H	E	D	F	R	A	M	H	V	N	G	V	Q	N	128		
1470	GAT	CTC	GTT	TCT	ACT	TTT	CCT	AAT	TAC	CTT	ATA	TCT	ATA	CTT	GAG	TCA	AAA	AAT	TGG	CAA	1529
129	D	L	V	S	T	F	P	N	Y	L	I	S	I	L	E	S	K	N	W	Q	148
1530	CTT	TTG	TTA	GAA	AT	gtaaata	accggtta	agatgt	tgcgcac	tttga	acaagact	gacaagt	atag	T	ATC	GGC	1601				
149	L	L	L	E	I									I	G	155					
1602	AGT	GAT	GCC	ATG	CAT	TAC	TTA	TTA	TCC	AAA	GGA	AGT	ATT	TTT	GAG	GCT	CTT	CCA	AAT	GAC	1661
156	S	D	A	M	H	Y	L	L	S	K	G	S	I	F	E	A	L	P	N	D	175
1652	AAT	TAC	CTT	CAG	ATT	TCT	GGC	ATA	CCA	CTT	TTT	AAA	AAT	AAT	GTG	TTT	GAG	GAA	ACT	GTG	1721
176	N	Y	L	Q	I	S	G	I	P	L	F	K	N	N	V	F	E	E	T	V	195
1722	TCA	AAA	AAA	AGA	AAG	CGA	ACC	ATT	GAA	ACA	TCC	ATT	ACT	CAA	AAT	AAA	AGC	GCC	CGC	AAA	1781
196	S	K	K	R	K	R	T	I	E	T	S	I	T	Q	N	K	S	A	R	K	215
1782	GAA	GTT	TCC	TGG	AAT	AGC	ATT	TCA	ATT	AGT	AGG	TTT	AGC	ATT	TTT	TAC	AGG	TCA	TCC	TAT	1841
216	E	V	S	W	N	S	I	S	I	S	R	F	S	I	F	Y	R	S	S	Y	235
1842	AAG	AAG	TTT	AAG	CAA	G	gtaacta	tactgtt	atccttc	ataacta	aattttag	AT	CTA	TAT	TTT	AAC	1907				
236	K	K	F	K	Q	D										L	Y	F	N	245	
1908	TTA	CAC	TCT	ATT	TGT	GAT	CGG	AAC	ACA	GTA	CAC	ATG	TGG	CTT	CAA	TGG	ATT	TTT	CCA	AGG	1967
246	L	H	S	I	C	D	R	N	T	V	H	M	W	L	Q	W	I	F	P	R	265
1968	CAA	TTT	GGA	CTT	ATA	AAC	GCA	TTT	CAA	GTG	AAG	CAA	TTG	CAC	AAA	GTG	ATT	CCA	CTG	GTA	2027
266	Q	F	G	L	I	N	A	F	Q	V	K	Q	L	H	K	V	I	P	L	V	285
2028	TCA	CAG	AGT	ACA	GTT	GTG	CCC	AAA	CGT	CTC	CTA	AAG	GTA	TAC	CCT	TTA	ATT	GAA	CAA	ACA	2087
286	S	Q	S	T	V	V	P	K	R	L	L	K	V	Y	P	L	I	E	Q	T	305
2088	GCA	AAG	CGA	CTC	CAT	CGT	ATT	TCT	CTA	TCA	AAA	GTT	TAC	AAC	CAT	TAT	TGC	CCA	TAT	ATT	2147
306	A	K	R	L	H	R	I	S	L	S	K	V	Y	N	H	Y	C	P	Y	I	325
2148	GAC	ACC	CAC	GAT	GAT	GAA	AAA	ATC	CTT	AGT	TAT	TCC	TTA	AAG	CCG	AAC	CAG	GTG	TTT	GCG	2207
326	D	T	H	D	D	E	K	I	L	S	Y	S	L	K	P	N	Q	V	F	A	345
2208	TTT	CTT	CGA	TCC	ATT	CTT	GTT	CGA	GTG	TTT	CCT	AAA	TTA	ATC	TGG	GGT	AAC	CAA	AGG	ATA	2267
346	F	L	R	S	I	L	V	R	V	F	P	K	L	I	W	G	N	Q	R	I	365
2268	TTT	GAG	ATA	ATA	TTA	AAA	G	gtattgt	ataaaatt	tattacc	actaacg	attttacc	ag	AC	CTC	GAA	ACT	2336			
366	F	E	I	I	L	K	D									L	E	T	375		

FIGURE 46 (cont.)

2337 TTC TTG AAA TTA TCG AGA TAC GAG TCT TTT AGT TTA CAT TAT TTA ATG AGT AAC ATA AAG 2396  
376 F L K L S R Y E S F S L H Y L M S N I K 395

2397 gtaatatgccaaattttttaccattaattaacaatcag ATT TCA GAA ATT GAA TGG CTA GTC CTT GGA 2465  
396 I S E I E W L V L G 405

2466 AAA AGG TCA AAT GCG AAA ATG TGC TTA AGT GAT TTT GAG AAA GCG AAG CAA ATA TTT GCG 2525  
406 K R S N A K M C L S D F E K R K Q I F A 425

2526 GAA TTC ATC TAC TGG CTA TAC AAT TCG TTT ATA ATA CCT ATT TTA CAA TCT TTT TTT TAT 2585  
426 E F I Y W L Y N S F I I P I L Q S F F Y 445

2586 ATC ACT GAA TCA AGT GAT TTA CGA AAT CGA ACT GTT TAT TTT AGA AAA GAT ATT TGG AAA 2645  
446 I T E S S D L R N R T V Y F R K D I W K 465

2646 CTC TTG TGC CGA CCC TTT ATT ACA TCA ATG AAA ATG GAA GCG TTT GAA AAA-ATA AAC GAG 2705  
466 L L C R P F I T S M K M E A F E K I N E 485

2706 gtatttttaagattttttgcaaaagctaatttttcag AAC AAT GTT AGG ATG GAT ACT CAG AAA ACT 2775  
486 N N V R M D T Q K T 495

2776 ACT TTG CCT CCA GCA GTT ATT CGT CTA TTA CCT AAG AAG AAT ACC TTT CGT CTC ATT ACG 2835  
496 T L P P A V I R L L P K K N T F R L I T 515

2836 AAT TTA AGA AAA AGA TTC TTA ATA AAG gtattaatttttggatcatcaatgtaactttacttctaattctatta 2906  
516 N L R K R F L I K 524

2907 ttagcag ATG GGT TCA AAC AAA AAA ATG TTA GTC AGT ACG AAC CAA ACT TTA CGA CCT GTG 2967  
525 M G S N K K M L V S T N Q T L R P V 542

2968 GCA TCG ATA CTG AAA CAT TTA ATC AAT GAA GAA AGT AGT GGT ATT CCA TTT AAC TTG GAG 3027  
543 A S I L K H L I N E E S S G I P F N L E 562

3028 GTT TAC ATG AAG CTT CTT ACT TTT AAG AAG GAT CTT CTT AAG CAC CGA ATG TTT GG gtaat 3088  
563 V Y M K L L T F K K D L L K H R M F G 581

3089 tatataatgcgcgatttcctcattattaattttgcag G CGT AAG AAG TAT TTT GTA CGG ATA GAT ATA 3155  
582 R K K Y F V R I D I 591

3156 AAA TCC TGT TAT GAT CGA ATA AAG CAA GAT TTG ATG TTT CGG ATT GTT AAA AAG AAA CTC 3215  
592 K S C Y D R I K Q D L M F R I V K K K L 611

3216 AAG GAT CCC GAA TTT GTA ATT CGA AAG TAT GCA ACC ATA CAT GCA ACA AGT GAC CGA GCT 3275  
612 K D P E F V I R K Y A T I H A T S D R A 631

3276 ACA AAA AAC TTT GTT AGT GAG GCG TTT TCC TAT T gtaagtttattttttcattggaattttttaacaa 3343  
632 T K N F V S E A F S Y F 643

3344 attcttttttag TT GAT ATG GTG CCT TTT GAA AAA GTC GTG CAG TTA CTT TCT ATG AAA ACA 3405  
644 D M V P F E K V V Q L L S M K T 659

3406 TCA GAT ACT TTG TTT GTT GAT TTT GTG GAT TAT TGG ACC AAA AGT TCT TCT GAA ATT TTT 3465  
660 S D T L F V D F V D Y W T K S S E I F 679

3466 AAA ATG CTC AAG GAA CAT CTC TCT GGA CAC ATT GTT AAG gtataccaattgttgtaattgtaataaca 3532  
680 K M L K E H L S G H I V K 692

# FIGURE 46 (cont.)

3533	ctaataaactag	ATA GGA AAT TCT CAA TAC CTT CAA AAA GTT GGT ATC CCT CAG GGC TCA	3593
693	I G N S Q Y L Q K V G I P Q G S		708
3594	ATT CTG TCA TCT TTT TTG TGT CAT TTC TAT ATG GAA GAT TTG ATT GAT GAA TAC CTA TCG		3653
709	I L S S F L C H F Y M E D L I D E Y L S		728
3654	TTT ACG AAA AAG AAA GGA TCA GTG TTG TTA CGA GTA GTC GAC GAT TTC CTC TTT ATA ACA		3713
729	F T K K K G S V L L R V V D D F L F I T		748
3714	GTT AAT AAA AAG GAT GCA AAA AAA TTT TTG AAT TTA TCT TTA AGA G gtgagttgctgtcattcc		3777
749	V N K K D A K K F L N L S L R G		764
3778	taagttctaaccgttgaag	GA TTT GAG AAA CAC AAT TTT TCT ACG AGC CTG GAG AAA ACA GTA	3840
765	F E K H N F S T S L E K T V		778
3841	ATA AAC TTT GAA AAT AGT AAT GGG ATA ATA AAC AAT ACT TTT TTT AAT GAA AGC AAG AAA		3900
779	I N F E N S N G I I N N T F P N E S K K		798
3901	AGA ATG CCA TTC TTC GGT TTC TCT GTG AAC ATG AGG TCT CTT GAT ACA TTG TTA GCA TGT		3960
799	R M P F F G F S V N M R S L D T L L A C		818
3961	CCT AAA ATT GAT GAA GCC TTA TTT AAC TCT ACA TCT GTA GAG CTG ACG AAA CAT ATG GGG		4020
819	P K I D E A L F N S T S V E L T K H M G		838
4021	AAA TCT TTT TTT TAC AAA ATT CTA AG gtatactgtgtaactgaataatagctgacaaataatcag	A TCG	4089
839	K S F F Y K I L R	S	848
4090	AGC CTT GCA TCC TTT GCA CAA GTA TTT ATT GAC ATT ACC CAC AAT TCA AAA TTC AAT TCT		4149
849	S L A S F A Q V F I D I T H N S K F N S		868
4150	TGC TGC AAT ATA TAT AGG CTA GGA TAC TCT ATG TGT ATG AGA GCA CAA GCA TAC TTA AAA		4209
869	C C N I Y R L G Y S M C M R A Q A Y L K		888
4210	AGG ATG AAG GAT ATA TTT ATT CCC CAA AGA ATG TTC ATA ACG G gtgagtacttattttaactaga		4274
889	R M K D I F I P Q R M F I T D		903
4275	aaagtcattaattaaccttag	AT CTT TTG AAT GTT ATT GGA AGA AAA ATT TGG AAA AAG TTG GCC	4339
904	L L N V I G R K I W K K L A		917
4340	GAA ATA TTA GGA TAT ACG AGT AGG CGT TTC TTG TCC TCT GCA GAA GTC AAA TG gtacgtgtc		4401
918	E I L G Y T S R R F L S S A E V K W		935
4402	ggctcgcagacttcagcaatattgacacatcag	G CTT TTT TGT CTT GGA ATG AGA GAT GGT TTG AAA	4468
936	L F C L G M R D G L K		946
4469	CCC TCT TTC AAA TAT CAT CCA TGC TTC GAA CAG CTA ATA TAC CAA TTT CAG TCA TTG ACT		4528
947	P S F K Y H P C F E Q L I Y Q F Q S L T		966
4529	GAT CTT ATC AAG CCG CTA AGA CCA GTT TTG CGA CAG GTG TTA TTT TTA CAT AGA AGA ATA		4588
967	D L I K P L R P V L R Q V L F L H R R I		986
4589	GCT GAT TAA tgcattttcaattttatatacatcctttattactgggtgtccttaacaatattattactaagtata		4665
987	A D *		989

FIGURE 46 (cont.)

4666 gctgacccccaaagcaagcatactataggattttctagtaaagtaaaattaatctcgttattagttttgattgacttgctc 4745  
 4746 ttatccttatacttttaagaaagattgacagtggttgcctgactactgccacatgccattaaacgggagtggttaaaca 4825  
 4826 ttaaagtaatacatgaggctaactctcctttcatttagaataaggaaagtgggttttctataatgaataatgccgcacta 4905  
 4906 atgcaaaaagacgaagattatcttctaacaagggggattaagcatatccgaaggaaaagagagtaatataccagtggtt 4985  
 4986 gttgaagaagcaaggataaatttgaacaagcttctgcagatgacaggcctaaattttggtgaccgaattttggtaaaagc 5065  
 5066 cccaggttatccatggtggcggccttgctactgagacgaaaagaaactaaggatagtttgaatactaatagtctcattta 5145  
 5146 atgtcttatataaggtttttgttttttctgacttcaattttgcatgggtgaaaagaaatagtgttaagccattattggat 5225  
 5226 tcgaaaatagccaaatttcttggttccctcaaagcgggaagtc taaagaacttattgaagcttatgaggcttcaaaaactcc 5305  
 5306 tcctgatttaaaggaggaatcttccaccgatgaggaaatggatagcttatcagctgctgaggagaagcctaatttttgc 5385  
 5386 aaaaaagaaaatcatctgggagacatctcttgatgaatcagatgcggagagatctccagcgatccttgatgtcaata 5465  
 5466 acttctattttctgaaatgtatggtcctactgtcgcttcgacttctcgtagctctacgcagtttaagtgaacaaaggtacc 5544

5544  
 5465  
 5385  
 5305  
 5225  
 5145  
 5065  
 4985  
 4905  
 4825  
 4745

FIGURE 47

1  
 met ser val tyr val val glu leu leu  
 ATG AGT GTG TAC GTC GTC GAG CTG CTC

10  
 arg ser phe phe tyr val thr glu thr thr phe gln lys asn arg  
 AGG TCT TTC TTT TAT GTC ACG GAG ACC ACG TTT CAA AAG AAC AGG

30  
 leu phe phe tyr arg lys ser val trp ser lys leu gln ser ile  
 CTC TTT TTC TAC CGG AAG AGT GTC TGG AGC AAG TTG CAA AGC ATT

40  
 gly ile arg gln his leu lys arg val gln leu arg glu leu ser  
 GGA ATC AGA CAG CAC TTG AAG AGG GTG CAG CTG CGG GAG CTG TCG

60  
 glu ala glu val arg gln his arg glu ala arg pro ala leu leu  
 GAA GCA GAG GTC AGG CAG CAT CGG GAA GCC AGG CCC GCC CTG CTG

70  
 thr ser arg leu arg phe ile pro lys pro asp gly leu arg pro  
 ACG TCC AGA CTC CGC TTC ATC CCC AAG CCT GAC GGG CTG CGG CCG

90  
 ile val asn met asp tyr val val gly ala arg thr phe arg arg  
 ATT GTG AAC ATG GAC TAC GTC GTG GGA GCC AGA ACG TTC CGC AGA

100  
 glu lys ala glu arg leu thr ser arg val lys ala leu phe  
 GAA AAG ARG GCC GAG CGT CTC ACC TCG AGG GTG AAG GCA CTG TTC

120  
 ser val leu asn tyr glu arg ala arg arg pro gly leu leu gly  
 AGC GTG CTC AAC TAC GAG CGG GCG CGG CGC CCC GGC CTC CTG GGC

130  
 ala ser val leu gly leu asp asp ile his arg ala trp arg thr  
 GCC TCT GTG CTG GGC CTG GAC GAT ATC CAC AGG GCC TGG CGC ACC

140  
 phe val leu arg val arg ala gln asp pro pro pro glu leu tyr  
 TTC GTG CTG CGT GTG CGG GCC CAG GAC CCG CCG CCT GAG CTG TAC

150  
 phe val lys val asp val thr gly ala tyr asp thr ile pro gln  
 TTT GTC AAG GTG GAT GTG ACG GGC GCG TAC GAC ACC ATC CCC CAG

180  
 asp arg leu thr glu val ile ala ser ile ile lys pro gln asn  
 GAC AGG CTC ACG GAG GTC ATC GCC AGC ATC ATC AAA CCC CAG AAC

00762537 004007



10  
9  
8  
7  
6  
5  
4  
3  
2  
1

370 380  
arg leu lys cys his ser leu phe leu asp leu gln val asn ser  
CGG CTG AAG TGT CAC AGC CTG TTT CTG GAT TTG CAG GTG AAC AGC

FIGURE 47 (cont.)

390  
 leu gln thr val cys thr asn ile tyr lys ile leu leu leu gln  
 CTC CAG ACG GTG TGC ACC AAC ATC TAC AAG ATC CTC CTG CTG CAG

400  
 ala tyr arg phe his ala cys val leu gln leu pro phe his gln  
 GCG TAC AGG TTT CAC GCA TGT GTG CTG CAG CTC CCA TTT CAT CAG

420  
 gln val trp lys asn pro his phe ser cys ala ser ser leu thr  
 CAA GTT TGG AAG AAC CCA CAT TTT TCC TGC GCG TCA TCT CTG ACA

430  
 arg leu pro leu leu leu his pro glu ser gln glu arg arg asp  
 CGG CTC CCT CTG CTA CTC CAT CCT GAA AGC CAA GAA CGC AGG GAT

440  
 val ala gly gly gln gly arg arg arg pro ser ala leu arg gly  
 GTC GCT GGG GGC CAA GGG CGC CGC CGG CCC TCT GCC CTC CGA GGC

450  
 arg ala val ala val pro pro ser ile pro ala gln ala asp ser  
 CGT GCA GTG GCT GTG CCA CCA AGC ATT CCT GCT CAA GCT GAC TCG

460  
 thr pro cys his leu arg ala thr pro gly val thr gln asp ser  
 ACA CCG TGT CAC CTA CGT GCC ACT CCT GGG GTC ACT CAG GAC AGC

470  
 pro asp ala ala glu ser glu ala pro gly asp asp ala asp cys  
 CCA GAC GCA GCT GAG TCG GAA GCT CCC GGG GAC GAC GCT GAC TGC

480  
 pro gly gly arg ser gln pro gly thr ala leu arg leu gln asp  
 CCT GGA GGC CGC AGC CAA CCC GGC ACT GCC CTC AGA CTT CAA GAC

490  
 his pro gly leu met ala thr arg pro gln pro gly arg glu gln  
 CAT CCT GGA CTG ATG GCC ACC CGC CCA CAG CCA GGC CGA GAG CAG

500  
 thr pro ala ala leu ser arg arg ala tyr thr ser gln gly gly  
 ACA CCA GCA GCC CTG TCA CGC CGG GCT TAT ACG TCC CAG GGA GGG

510  
 arg gly gly pro his pro gly leu his arg trp glu ser glu ala  
 AGG GGC GGC CCA CAC CCA GGC CTG CAC CGC TGG GAG TCT GAG GCC

520  
 560  
 arg gly gly pro his pro gly leu his arg trp glu ser glu ala  
 AGG GGC GGC CCA CAC CCA GGC CTG CAC CGC TGG GAG TCT GAG GCC

530  
 564  
 OP  
 TGA GTGAGTGTTTTGGCCGAGGCCTGCATGTCCGGCTGAAGGCTGAGTGTCCGGCTGAGG  
 CTGAGCGAGTGTCCAGCCAAGGGCTGAGTGTCCAGCACACCTGCGTTTTCACCTTCCCCAC

FIGURE 47 (cont.)

AGGCTGGCGTTCGGTCCACCCAGGGCCAGCTTTTCTCACCAGGAGCCCGGCTTCCACT  
CCCCACATAGGAATAGTCCATCCCCAGATTGCGCATTTGTTACCCCTTCGCCCTGCCTTCC  
TTTGCCCTTCCACCCCAACATTTCAGGTGGAGACCCTGAGAAGGACCCTGGGAGCTTTGGG  
AATTTGGAGTGACCAAGGTGTGCCCTGTACACAGGCGAGGACCCTGCACCTGGATGGGG  
GTCCCTGTGGGTCAAATTGGGGGGAGGTGCTGTGGGAGTAAAATACTGAATATATGAGTT  
TTTCAGTTTGGAAAAAAAAAAAAAAAAAAAAAAAAAAAA

5076227.07102

FIGURE 48

Motif -1  
Ep p123 ...LVVSLIRCFYVTEQQKSYSKT...  
Sp Tez1 ...FIIPILQSFFYITESSDLRNRT...  
Sc Est2 ...LIPKIIQTFYCYCTEISSVTIV...  
Hs TCP1 ...YVVELLRSFFYVTETTFQKNRL...  
consensus FFY TE

Motif 0  
p hhh K hR h R  
Ep p123 ...KSLGFAPGKLRLLIPKKT--TFRPIMTFNKKIV...  
Sp Tez1 ...QKTTLPPAVIRLLPKKN--TFRLITNLRKRFL...  
Sc Est2 ...TLSNFNHSMRIIPKKSNNEFRIIAIPCRGAD...  
Hs TCP1 ...ARPALLTSRLRFIPKPD--GLRPVNM DYVVG...  
consensus R PK RI

Motif A  
h hDh GY h  
Ep p123 ...PKLFFATMDIEKCYDSVNREKLSTFLK...  
Sp Tez1 ...RKKYFVRIDIKSCYDRIKQDLMFRIVK...  
Sc Est2 ...PELYFMKFDVKSCYDSIPRMECMRILK...  
Hs TCP1 ...PELYFVKVDVTGAYDTIPQDRLTEVIA...//...  
consensus F D YD

Motif B  
hPQG pS hh  
Ep p123 ...NGKFYKQTKGIPQGLCVSSILSSFYYA...  
Sp Tez1 ...GNSQYLQKVGIPQGSILSSFLCHFMYE...  
Sc Est2 ...EDKCYIREDGLFQGSLSAPIVDLVYD...  
Hs TCP1 ...RATSYVQCQGIPQGSILSTLLCSLCYG...  
consensus G QG S

Motif C  
Y  
h F DDhhh  
Ep p123 ...PNVNLLMRLTDDYLLITTQENN...  
Sp Tez1 ...KKGSVLLRVVDDFLFITVNKKD...  
Sc Est2 ...SQDTLILKLADDFLIISTDQQQ...  
Hs TCP1 ...RRDGLLLRLVDDFLLVTPHLTH...  
consensus DD L

Motif D  
Gh h cK  
Ep p123 ...NVSRENGFKFNMKKL...  
Sp Tez1 ...LNLSLRGFEKHNFST...  
Sc Est2 ...KKLAMGGFQKYNKA...  
Hs TCP1 ...LRTLVRGVPEYGCVV...  
consensus G